Recent advances in the application of capillary electromigration methods for food analysis and Foodomics

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Abbreviations: AD, amperometric detection; **BAs**, biogenic amines; **CSI**, cation-selective injection**; C4D**, capacitively coupled contactless conductivity; **DAPM**, 4,4'-diaminophenylmethane; **DAT**, 2,4-diaminotoluene; **DLLME**, dispersive liquid-liquid microextraction; **2D**, two-dimensional; **ED**, electrochemical detection; **FAD**, flavin adenine dinucleotide disodium; **FASS**, field-amplified sample stacking; **FESI**, field-enhanced sample injection; **FMN**, flavin mononucleotide sodium; **FQs,** fluoroquinilones; **GM**, genetically modified; **GMO**, genetically modified organism, **HAs**, heterocyclic amines; **HMF**, 5-Hydroxymethylfurfural; **HMW**, highmolecular-weight; **LED-COF**, light-emitting diode with cyclindrical optical fiber; **LED-TOF**, light-emitting diode with tapered optical fiber; **LLE**, liquid-liquid extraction; **MLGA**, multiplex ligation-dependent genome amplification; **MLPA**, multiplex ligation-dependent probe amplification; **MPIC**, microdroplet PCR implemented capillary gel electrophoresis; **MRLs**, maximum residue limits; **MSPE**, magnetic solid phase extraction; **NSM**, normal stacking mode; **PA-FESI**, pressure-assisted field-enhanced sample injection; **PGD**, potential gradient detection; **PLE**, pressure liquid extraction; **PMME**, poly(methacrylic acid-co-ethylene glycol dimethacrylate; **QD**, quantum dots; **RFLP**, restriction fragment length polymorphism; **tITP**, transient isotachophoresis; **REPSM**: reversed electrode polarity stacking mode.

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Abstract

Analysis of foods an food components using capillary electromigration methods is reviewed in this work. Papers that were published from February 2009 to February 2011 are included following the previous review by Herrero et al. (*Electrophoresis*, 2010, 31, 205–228). Analysis of amino acids, biogenic amines, peptides, proteins, DNAs, carbohydrates, phenols, polyphenols, pigments, toxins, pesticides, vitamins, additives, small organic and inorganic ions and other compounds found in foods and beverages are reviewed, as well as those applications of CE for monitoring food interactions and food processing. The use of microchips, CE-MS and chiral-CE in food analysis is also discussed as well as other current and foreseen trends in this area of research including new developments in Foodomics.

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1. Introduction

Analysis of foods is continuously demanding the development of robust, efficient, sensitive and cost-effective analytical methodologies to guarantee the safety, quality and traceability of foods in compliance with legislation. Currently, there is also a growing deal of research on nutritional and, mainly, functional properties of foods as a result of an increasing public concern on how to improve health through the so called functional foods, functional ingredients and nutraceuticals [1].

Among the different analytical separation techniques used for food analysis, capillary electrophoresis (CE) has been established as a versatile and robust tool providing fast, efficient and automated separations with small sample volumes and low consumption of solvents and reagents. The present review focuses on recent developments and applications of CE to detect compounds of significance to food science and technology, covering the literature published from February 2009 to February 2011, following the previous review by our group [2]. In the mentioned period, several reviews have been published describing different applications of CE to analyze specific groups of compounds with potential interest in food analysis and/or Foodomics [3]. Table 1 shows a summary of these review papers [4-26]. As can be seen, CE has been applied to analyze contaminants [5, 10, 13, 16, 17, 18, 24], chiral compounds [11, 15], polyphenols [8, 9, 12, 25] amino acids [14], nucleosides and nucleotides [19] in different foods.

Other important topics that have been reviewed have been the use of miniaturized methodologies including CE for food analysis [7], chemiluminescence coupled to CE [20], or different sample preparation and stacking procedures prior to CE [21, 22]. Besides, CE alone or combined with mass spectrometry has been applied to analyze

genetically modified crops [4, 26] as well as for other food issues including food safety and quality [6] or food authentication and traceability [23].

The present work will focus on the main CE applications performed in Food Science and Technology including the new field of Foodomics [3] reviewing recent results on quality control and safety, nutritional value, processing effects, storage, bioactivity, etc. The CE analysis of a large variety of food related molecules with different chemical properties, including amino acids, peptides, proteins, phenolic compounds, carbohydrates, DNA fragments, vitamins, toxins, pesticides, additives and chiral compounds is described in the following sections.

2. Amino acids, biogenic amines, heterocyclic amines and other hazardous amines

Although LC and GC are two of the most used analytical platforms for amino compounds analysis, CE has demonstrated to be also very useful since it is cost-effective, rapid and reliable for analysis of amino compounds. Analysis of amino acids in foods is useful for a variety of issues, including nutritional information, processing/storage, authenticity and quality control, among others. A review showing the potential of MEKC for the determination of amino acids has been published recently [14]. Analysis of amino acids is usually preceded by a derivatization step using a suitable chromophore or fluorophore, although the use of mass spectrometry or an alternative detection mode could skip this derivatization step. Thus, Zinellu et al. developed a CZE-LIF method for the determination of the non-proteinic amino acid taurine derivatized with FITC [27]. After separation and derivatization optimization, the new method was useful for the determination of taurine in biological

fluids and food samples, more precisely, an energy drink and milk. Using this method, taurine was analyzed in less than 10 min with LOQ of 1 μM.

An important indicator of food quality and freshness is the analysis of biogenic amines (BAs). BAs are derived mainly from amino acids through substrate-specific decarboxylase enzymes. The excessive amount intake of these nitrogenous compounds may produce a variety of symptoms including headache, diarrhea, vomiting. Recently, Baskan et al. reported the MEKC-LIF analysis of a group of BAs (histamine, putrescine, cadaverine, tyramine, tryptamine and spermidine) in salted fish samples (**Figure 1**) [28]. The novelty of the method consisted on the use of the non-ionic surfactant Brij 35 instead of SDS in the separation electrolyte, which enhanced fluorescent intensity of FITC-labeled BAs and shortened separation time to 10 min. Dossi et al. applied a new developed approach consisting on the use of end-channel amperometric detectors in microchip CE to the analysis of BAs and their amino acid precursors in double malt dark beers (see below CE microchip technology in food analysis section) [29].

Heterocyclic amines (HAs) are another important group of compounds with serious health risk for the population. They are formed from amino acids, creatine/creatinine, and sugar during cooking of fish and meat at high temperatures. Analytical determination of HAs is of major importance since their intake may increase the risk of a number of cancer diseases. De Andres et al. combined supercritical fluid extraction procedure for HAs extraction from cooked meat samples with CZE-LIF analysis [30]. LODs ranging from 15.9 to 28.1 ng/mL were obtained for a group of six non-polar HAs in less than 13 min of separation analysis.

Wang et al. developed a CZE-UV method for the analysis of primary aromatic amines (aniline, 4,4’-diaminophenylmethane (DAPM), 2,4-diaminotoluene (DAT)) in

foodstuffs [31]. Melamine was also included in this work since is a common compound in various adhesives. The method included a transient isotachophoresis (tITP) stacking process to achieve a LOD of 0.242 µg/g for melamine in milk powders. On the other hand, after the analysis by tITP–CE–UV of migrates from composite food packaging bags LODs were 0.40, 0.62, 0.47 and 0.63 µg/mL for DAPM, DAT, aniline and melamine, respectively. Melamine is also a potent adulterant agent. In 2008, a variety of Chinese milk-related products were found to contain melamine, added to fraudulently increase the nitrogen content of milk causing a mass poisoning with severe kidney damages [32]. As a consequence, a notable number of works have been published in the last years regarding the determination of melamine in foods. Several CZE methods using UV or DAD detection have been developed. Xia et al. analyzed melamine and related compounds (ammeline, ammelide and cyanuric acid) in less than 10 min using an uncoated silica capillary and 40 mM disodium hydrogen phosphate buffer at pH 9.0 as BGE [33]. Several foods, including milk powder, yoghurt, milk and ice-cream were analyzed obtaining LODs lower than 0.059, 0.302, 0.342 and 0.235 µg/g for melamine, ammeline, ammelide and cyanuric acid, respectively. Acidic buffer composed of 50 mM sodium dihydrogen phosphate at pH 3.1 was selected for the analysis of cyromazine and melamine by CZE [34]. Very good resolution of these two compounds was obtained in less than 7 min of separation. The developed method was applied to the quantification of cyromazine and melamine residues in a variety of food matrices, obtaining LODs of 0.12 µg/g for pig feed samples and 0.13 µg/g for egg and liquid milk samples. Similar analysis conditions using acidic buffer as BGE were used by Wen et al. for CZE determination of melamine in milk powder, milk and fish feed in less than 7 min [35]. The calculated LOD was in this case 0.08 µg/g. Meng et al.

developed also a very fast CZE-UV analysis of melamine (in less than 2 min) using an alkaline BGE (30 mM sodium tetraborate at pH 9.3) [36]. Melamine was preconcentrated with SPE prior to CE analysis. The calculated LOD was between 0.25 and 0.5 μg/g for different kinds of toxic-free foods from local supermarket (wheat protein, chicken meat, fish meat, milk, eggs) spiked with melamine. MS detection has also been described after CZE separation of melamine. Although LOD (0.25 μg/g) was similar to those obtained with UV detection, MS provided the unambiguous assignment of peaks particularly in complex food matrices [37].

A MEKC method was developed for the determination of melamine and its related by-products (ammeline, ammelide and cyanuric acid) in samples of flour by Hsu et al. [38]. To improve the detection sensitivity, reversed electrode polarity stacking mode (REPSM) and cation-selective injection (CSI) were employed as on-line preconcentration steps. LODs of 2.8 μg/L and 2.4-5.0 μg/L for melamine and its by-products, respectively, were achieved under optimal conditions.

3. Peptides and proteins

Peptides and protein content affect both functional and biological properties of foods. One of the main difficulties of proteins analysis by CE is the detrimental effect of their adsorption onto the inner capillary wall that results in band broadening and decreasing of separation efficiency. The use of silica capillary coatings and optimization of BGE composition improve resolution allowing better resolution of complex protein mixtures. Peláez-Lorenzo et al. developed a fast sample preparation method for the subsequent CE-LIF analysis of β-lactoglobulin in baby foods contaminated with different dairy products [39]. Sample preparation consisted on a

first step of lipid removal suspending the baby food in phosphate buffer saline (PBS). Extraction of β-lactoglobulin was carried out adding to this suspension a solution containing 24 mM mercapthoethanol, 25 mM guanidine hydrochloride, and 5% of 2.5 mM borate buffer at a final pH of 7.3, and a 0.15 M sodium chloride solution. After shaking and centrifugation, the supernatant was filtered and analyzed by CE-LIF. Using this procedure, levels of contamination as low as one part of yoghurt in 10000 parts of baby food could be detected.

Vallejo-Cordoba et al. proposed a SDS-CGE-UV separation method for meat species identification for quality control purposes [40]. Here, characterization and comparison of water soluble and salt soluble protein fractions from bovine and ostrich tissues, was performed. Separation of the proteins was carried out on the basis of their molecular weights using a commercial BGE that produced a dynamic sieving effect. Polyethylene oxide (PEO) polymer was also used as a sieving agent for the separation of high molecular-weight (HMW) secalin and glutenins subunits from triticale, a hybrid of wheat and rye, suitable as animal feed and for human consumption [41]. Compared to traditional SDS-PAGE, the obtained higher resolution of the proposed CGE method allowed a better qualitative and quantitative composition of HMW secalins and glutenins in triticale seeds that can be used as a tool to improve this particular cultivar.

Protein profiles from olive oil were obtained by Montealegre et al. by CZE-UV [42]. The developed method was used to carry out the differentiation of monovarietal olive oils. A simple extraction procedure with cold acetone enabled the isolation of proteins from the lipidic matrix. On the other hand, a pre-coating polymer using a commercially available linear acrylamide-based polymer solution was needed in order to avoid protein adsorption onto the inner capillary wall and to reduce EOF.

Proteolysis plays an important role during ripening of cheese. This process is directly related to flavor and texture of cheese. CZE-UV was used for the characterization of the casein fraction of cheeses with different stages of ripening [43]. It was observed that in a first stage of ripening the proteolysis of β-casein occurred faster than αs1-casein. However, at the end of ripening (day 90) αs1-casein suffered higher proteolytic degradation, since in the last days the proteolysis was more intense.

Peptides are in general better separated by LC and/or CE techniques and also more easily analyzed by MS than proteins. Peptidomic/proteomic CE-MS-based studies may be useful to understand protein composition. Many research works have been published in the past regarding the analysis of peptides displaying a variety of biological activities in dairy products. Recently Catala-Clariana et al. developed a CE-MS method for the separation and identification of bioactive peptides in milk-derived products [44]. Combining the information obtained by CE–IT-MS and CE–TOF-MS nine bioactive peptides with angiotensin-converting enzyme inhibitory activity were tentatively identified and 5 of them (i.e. LKP, IPY, ALPM, PGPIHN and VAGTWY) could be confirmed. In a recent work, Simó et al. presented a non-targeted proteomic work aimed to study the equivalence between a genetically modified (GM) transgenic soybean and its isogenic non-transgenic counterpart, in order to detect possible unintended effects [45]. Hence, in this work, proteins were extracted from both types of soybeans, enzymatically hydrolyzed and the resulting peptides analyzed by CE-TOF-MS. Results showed that no significant changes were found in the specific proteins fraction studied between the conventional and the GM soybean (**Figure 2**).

4. Phenols, polyphenols, and pigments

The term “phenolic compounds” encompasses a huge number (ca. 8000) of compounds occurring in natural sources with different chemical structures. Traditionally the interest in these compounds was mainly related to their organoleptic characteristics, such as colour, taste and flavor. However, nowadays they are receiving considerable interest for their health benefits, namely antioxidant, anti-inflammatory and anti-microbial effects as well as their role in the prevention of certain forms of cancers and cardiovascular diseases [8, 46].

Analysis of phenolic compounds is one of the main applications of CE in food analysis as can be deducted from the number of published works [47-71]. The main food matrices analyzed by CE for determining phenol, polyphenols, and pigments in the period of time covered by this review were olive oils [47-53], tea [54-59], and wine [60-62].

The determination of phenolic acid in olive oils has been carried out employing different CE and detection modes. Thus, the phenolic profiles of extra virgin olive oils have been studied by CZE [47] and CEC [48] with UV detection in order to classify the olive oils according to their geographical origin. Recently, a CZE-UV method for the separation and quantification of thirteen phenolic compounds, including tyrosol, hydroxytyrosol, oleuropein glycoside, ferrulic acid, *p*-coumaric acid, cinnamic acid, *p*-hydroxybenzoic acid, gallic acid, caffeic acid, luteolin, apigenin, vanillic acid and 3,4-dihydroxybenzoic acid, from extra-virgin olive oil has been published [49]. Under the separation conditions, which were optimized using multivariate statistical techniques considering variations in electrolyte concentration, pH and applied voltage, the separation was achieved in less than 14 min as can be seen in **Figure 3**. In addition, the use of stacking as preconcentration technique provided 4- and 6-fold enhancement in the peak height and areas, respectively. On the other hand, phenolic

compounds from olive oils have also been determined using MS as detection mode. Hydroxyphenylacetic acid, gentisic acid, ferulic acid, vanillic acid, and three isomer of coumaric acid were studied in the polar fraction (obtained by SPE) of extra and virgin olive oil from three different olive varieties by CE-MS with a co-axial sampling mode [50]. Later on, this research group employed an orthogonal sampling mode under the same separation conditions in order to improve the analytical results [51]. They demonstrated that the orthogonal position provided better repeatability and lower LODs (from 3.5-500 μg/L to 3-24 μg/L using co-axial and orthogonal sampling, respectively) than co-axial sampling mode. In a work by García-Villalba et al., a two-dimensional (2D)-HPLC-CE method was successfully applied to the characterization of the phenolic fraction of extra virgin olive oils [52]. These fractions were isolated using a semi-preparative HPLC in the first dimension, and analyzed by CE-MS in the second dimension. The quantification of several compounds in the polyphenolic profile and *in vitro* studies of their anti-cancer properties were carried out using some of the isolated fractions. Further investigations of the same group have demonstrated the potential of NACE coupled to MS to study the profile of phenolic fraction of extra virgin olive oil [53]. This method allows direct injection of olive oils in the capillary.

With regards to the determination of phenolic acids in tea, Hsiao et al. employed a MEKC-UV method for the quality control of tea fermentation [54]. To do that, they determined fourteen major compounds in tea (seven tea catechins, three xanthines, gallic acid, vitamin C, theanine and theaflavin) within 8 min using as running buffer 10 mM phosphate, 4 mM borate, 45 mM SDS and 0.5 % ethanol. In a work by Peres et al. a reduced flow MEKC-UV method was applied to the quantitative analysis of five cathechins in green tea infusion [55]. This methodology, based on the use of 0.2

% triethylamine, 50 mM SDS and sulphated-β-cyclodextrin, enabled to obtain the separation in less than 4 min with LODs between 0.02 and 0.1 μg/mL and recovery percentages of 94-101%. The addition of cyclodextrins to the BGE to improve the separation selectivity of phenolic acids and flavonoids has been also reported in other works. For instance, Chi et al. developed a CZE method with amperometric detection (AD) in which the phosphate buffer contained β-cyclodextrin for the simultaneous determination of kaempferol, apigenin, rutin, quercetin, luteolin and ferulic acid in Chinese herbal tea [56]. Cesla et al. demonstrated the suitability of a off-line 2D system combining HPLC (first dimension) and MEKC separation in borate buffer with SDS and heptakis-(6-*O*-sulfo)-β-cyclodextrin (second dimension) for the separation of twenty-five flavone compounds and phenolic acids [57]. On the other hand, Li et al. described for the first time, the use of microwave-assisted extraction followed by CZE-UV for the fast analysis of cathequin and epicatechin in green tea [58]. Uysal et al. carried out the separation of cathequins and methylxanthines, namely cathequin, epicatechin, epigallocatechin, theophylline and caffeine, in green and black tea by CEC within 30 min using a bidentate C18 column and 5 mM acetate buffer with water/ACN (80:20, v/v) as mobile phase [59].

Different phenolic compounds from wines have also been analysed by CE methods. Thus, stilbene resveratrol, phenolic acids (syringic, coumaric, caffeic and gallic acid) and flavonoids (catechin, rutin, kaempferol, myricetin, and quercetin) were simultaneously determined in wines using a CZE-UV method [60]. LODs from 0.1 to 0.3 mg/L were achieved under the best separation conditions, which were optimized using factorial design and response surface analysis. A simple CZE-UV method based on the use of 50 mM borate-10 mM phosphate buffer was successfully applied to the quantification of eight polyphenolic compounds in wine [61]. In this work, six wine

pre-treatments (two direct injections without extraction step, three liquid-liquid extraction (LLE), and a SPE procedure) were compared to find the most effective process for the isolation of polyphenolic compounds. Among them, LLE with diethyl ether as the organic solvent demonstrated to be the most effective method. Du and Fung carried out the determination of trans-resveratrol, catechin, epicatechin, quercetin and gallic acid in red wines within 16 min using a CE-dual opposite carbon fiber micro-disk electrode (DOCME) detection and demonstrated the applicability of this detection system for peak purity assessment [62].

Although most of the applications to the determination of phenols have been carried out in the samples described above, CE methods with different detection modes have also been reported in literature for the determination of these compounds in other natural samples. For instance, the development of CZE methodologies with UV detection have allowed the determination of bioactive components, including *trans*-resveratrol, astilbin, taxifolin, shikimic acid, syringic acid and ferulic acid in *Rhizoma Smilacis Glabrae* (one of the main ingredients in an old traditional functional food) [63], the separation and quantitation of phenolic acids (sinapic, ferulic, *p*-coumaric and caffeic acids) in broccoli, broccolini, Brussels sprouts, cabbage and cauliflower [64], the determination of free and bound phenolic acid in exotic fruits [65], or the analysis of bound phenolic acids in wheat varieties [66]. Besides, the evaluation of the antioxidative capability of phenolic compounds from an extract of eggplant skin was investigated by CZE-UV or HPLC-MS/MS [67]. CZE coupled with AD was employed for the simultaneous determination of six antioxidants, namely glutathione, ascorbic acid, vanillic acid, chlorogenic acid, salicylic acid and caffeic acid, in fruits and vegetables [68], CZE with electrochemical detection (ED) enabled the simultaneous determination of seven bioactive phenols (acacetin, scopoletin,

kaempferol, p-coumaric acid, vanillic acid, luteolin and quercetin) in the polar extract of *Fructus Lycci* [69], and a CZE method coupled to MS/MS detection was developed for the quantification of citrus flavonoids (naringin, neohesperidin, hesperidin and narirutin) in methanolic extract of sweet and bitter orange peel [70]. In addition, a pressurized liquid extraction (PLE) and CEC method with peak suppression diode array detection was optimized by Chen et al. for determining flavonoids, including liquiritin, isoliquiritin, ononin, liquiritigenin and isoliquiritigenin, in different species and parts of licorice (the dried roots and rhizomes of *Glycyrrhiza* species used as sweeteners) [71].

5. Carbohydrates

Carbohydrates are essential biomolecules in plants and animals since these compounds are energy and carbon sources required for metabolism. They constitute a large portion of our diet and they are involved in almost every aspect of human life. The diversity of monosaccharides and homologues coming from diverse linkage forms or from their combinations makes their analytical separation challenging. Besides, the lack of a chromophore group is an additional drawback for the electrophoretic determination of sugars. This problem is frequently solved using a stage of derivatization. For instance, a CZE method with UV detection has been used to study the composition of polysaccharide from the roots of Tibetan herb *Potentilla anserine L*, which is among the most popular health-promoting herbs in China [72]. In that work nine monosaccharides (xylose, arabinose, glucose, rhamnose, mannose, fucose, galactose, glucuronic acid, and galacturonic acid) were derivatizated with 1-naphthyl-3-methyl-5-pyrazolone (NMP) and separated in borate buffer within 16 min.

CE with LIF detection has also shown to be promising for the separation of 9-aminopyrene-1,4,6-trisulfonate (APTS)-galactooligosaccharides extracted from food matrices, such as infant formula, fruit juice and a maltodextrin-rich preparation, using a SPE with graphitized carbon cartridges in combination with an enzymatic amyloglucosidase pretreatment [73].

Another approach to solve the lack of chromophore groups in the carbohydrates structures consists on the use of indirect UV detection. Thus, Tezcan et al. investigated the composition of saccharides in pomegranates juices [74] and Turkish honeys [75] since the fructose/glucose ratio is an important fingerprint for detecting adulterations. To do that, the separation conditions were slightly modified from a method previously developed by the same group [76] using glycilglycine as the BGE improving the resolution of saccharides and indirectly detecting them at 350 nm. Fructose/glucose ratio was found within acceptable values for the honey samples [75] whereas a possible adulteration was detected in one of the pomegranate juice studied [74].

Different strategies have also been developed to enhance the UV direct detection of carbohydrates. Rovio et al. carried out the separation of carbohydrates, small organic and inorganic compounds in six grape red wines [77] using a previously developed CE method based on the in-capillary enodilate formation in a medium of extreme alkalinity (130 mM sodium-36 mM disodium hydrogen phosphate dihydrate buffer at pH 12.6) and direct UV detection at 270 nm [78]. Among the thirteen carbohydrates analyzed (including sugars alcohols, disaccharides, and monosaccharides), glucose, fructose and *myo*-inositol were found at the highest concentrations [77]. On the other hand, Alekseeva et al. studied the suitability of ligand-exchange CE for the determination of glucose, fructose and sucrose as corresponding complexes with Cu^{2+}

in fruit juices, wines and yoghurt enriched in calcium [79]. Under the optimal experimental conditions (1 mM Cu^{2+} in 175 mM ammonia) and direct UV detection at 254 nm, the LOD for glucose was 21 mg/L. This LOD was around 2.5 times higher than the LOD obtained using a CE-indirect UV detection method at 280 nm (working electrolyte containing 5 mM tryptophan and 50 mM sodium hydroxide). Althougth the LOD with indirect UV detection was lower, the method could be successfully applied to the analysis of carbohydrates in real samples since their levels in that samples were of several grams per liter.

Other detection modes such as capacitively coupled contactless conductivity (C^4D) or amperometric detection (AD) have also been used for the analysis of carbohydrates by CE [80, 81]. Thus, a CZE-C^4D method has been described for the detection of adulterations in instant coffee by the addition of coffee husks and corn by Nogueira and Lago [80]. In that work, xylose and glucose, which were obtained by acid hydrolysis of xylan and starch, respectively, present in the adulterants, were used as quality markers. Since the sugars are weak acids, their separation by CZE is possible using strong alkaline BGE (80 mM NaOH, 0.5 mM CTAB, 30 % MeOH). So the separation is based on their electrophoretic mobilities and they can be detected as negative peaks. As it can be observed in **Figure 4** the method allowed detecting the presence of xylose or glucose in coffee samples contaminated with coffee husks or corn grain. Regarding AD, a CE-AD (copper-disk electrode) method has been developed for the simultaneous determination of sugars (fructose, glucose, and sucrose), amino acids (L-glutamine and L-theanine), epigallocatechin gallate, and ascorbic acid in oolong tea infusion by using different buffers in detection and separation sections [81]. The separation capillary was filled with a mild alkaline borate-phosphate buffer (30 mM borate and 40 mM phostate at pH 8.5) at which the

compounds are negatively charged and the copper disk electrode was immersed in the detection cell filled with a strongly alkaline buffer (100 mM NaOH) to lead electrocatalysis oxidation of the analytes.

6. DNAs

Several CE-based approaches have been developed for DNA analysis in food. These applications include, e.g., food authenticity testing and the detection of genetically modified organisms (GMOs). Most of these studies were directed to increase throughput and reduce cost and time of analysis. The strategies developed to speed up the detection of target DNA sequences in foods include multiplexing the amplification process in order to increase as many as possible the number of target DNA sequences that can be simultaneously detected in a single analysis. Among the molecular techniques available for simultaneous detection, multiplex PCR has been the most widely explored for GMO analysis. Recently, Holck et al. have developed a novel multiplex-PCR using primers labeled with different fluorescent dyes that in combination with CGE-LIF enables the detection of five novel maize events in raw materials and feed [82]. However, conventional multiplex PCR suffers from several limitations including the preferential amplification of some target molecules, and the nonspecific amplification due to the interference of multiple primer pairs in a single reaction. Alternative techniques, such as ligation-based amplification and microdroplet-based PCR technology have been explored aimed at shortcoming the mentioned limitations of multiplex PCR. DNA ligation-based amplification techniques combine a ligation step, required for specificity, and an amplification step, required for sensitivity. Based on this idea, different techniques have been reported in

the last years. For instance, multiplex ligation-dependent probe amplification (MLPA) is based on the amplification of products resulting from the ligation of bipartite hybridization probes using universal amplification primers. A MLPA method has been developed for the quantitative determination of eight genetically modified maize lines [83]. Quantitative estimations were calculated based on normalization to a reference gene sequence under ligation and amplification conditions strictly optimized for the quantitative dynamic range (0-2% GMO) covered by the method. Using this approach an average regression coefficient of 0.95 ± 0.04 was obtained for the eight GMOs and the limit of detection was set at an average between 0.4 and 0.5% GMO. Recently, García-Cañas et al. have developed multiplex ligation-dependent genome amplification (MLGA) for the parallel amplification of multiple transgenic sequences in food samples [84]. MLGA technique, in contrast to the aforementioned ligation technique, is based on the ligation of genomic DNA instead of probe molecules and, a single specific probe (~ 80 nt) is required for each target. MLGA products obtained from reference materials were analyzed by CGE-LIF with YOPRO-1 dye providing good sensitivity for the simultaneous detection in a single run of percentages of transgenic maize as low as 1% of GA21, 1% of MON863, and 1% of MON810 in maize samples. In addition to this, CGE-LIF method demonstrated to be useful during optimization stage of the reaction conditions of the MLGA method (**Figure 5**). During development stage of MLGA method, stringent requirements on probe oligonucleotide quality and purity were evidenced for good method sensitivity and specificity. During MLGA method development, defects in the oligonucleotide sequence result in the loss of hybridization and ligation efficiencies. These defects, produced typically during solid-phase synthesis of long oligonucleotides, were overcome by developing an enzymatic procedure that was monitored by CGE-LIF

[85]. By means of a ligation reaction, long DNA probes were obtained from smaller oligonucleotides. The CGE-LIF method demonstrated to be very useful and informative for the characterization of the ligation reaction, providing important information about the nature of some impurities, as well as for the optimization of the ligation conditions.

Recently, microdroplet-based PCR has been combined with CGE-LIF as a potential technique for multiplex detection. The technique is named microdroplet PCR implemented capillary gel electrophoresis (MPIC) and is based on the amplification of single molecules in individual microdroplets, alleviating the above-described drawbacks of conventional multiplex PCR and allowing uniform and parallel amplification of numerous target sequences [86]. MPIC has been successfully applied to the simultaneous detection of 24 DNA target sequences of 14 GMOs. During method development stage parameters affecting the amplification and formation of emulsion droplets were optimized. Then, under optimal MPIC conditions, the applicability of the method was evaluated on samples containing different GMO contents. CE allowed the separation and detection of 24 different targets amplified from samples with contents as low as 0.1% GMO in a single run demonstrating the high-throughput potential of MPIC approach.

7. Vitamins

Vitamins are organic substances indispensable for the normal growth and function of human and animals. They cannot be produced within the body, with the exception of vitamin C, so they have to be obtained from the diet since the lack of vitamins can cause serious diseases. Food is the main resource of vitamins, which are divided

according to their solubility into two groups, water-soluble and fat-soluble vitamins. Within the period covered by this review, several CE methods have been developed for the analysis of water-soluble vitamins in food samples.

Folic acid is a form of the vitamin B_9, which is involved in the prevention of megaloblastic anemia. A CZE method was developed for the determination of folic acid in different variety of lentils [87]. After a simple extraction procedure, the analysis of folic acid was carried out using 10 mM borate in 10 % methanol at pH 9.0 and a detection wavelength at 200 nm achieving a LOD of 6×10^{-7} M. The amount of folic acid founded in three different varieties of lentils ranged from 0.408 to 0.742 mg/g.

Due to the fluorescent characteristics of riboflavin (vitamin B_2), it has been used as probe compound for the development of different approaches by CE with LIF detection. For instance, Yu at al. employed riboflavin, flavin mononucleotide sodium (FMN), and flavin adenine dinucleotide disodium (FAD) to evaluate a wall-free detection of CE-LIF method [88]. Authors fabricated a narrow gap between two capillaries with the polyimide coating sleeve and the liquid junction in the gap was adopted as the wall-free cell. The LOD obtained by wall-free cell were between 6 and 15 times lower than the LOD obtained with an on-column cell due to the enhanced light path and reduced optical noise. This methodology was applied to the quantification of riboflavin, FMN, and FAD in spinach and lettuce leaves [88]. On the other hand, Yang et al. used riboflavin as probe compound to study the effect of two different optical fibers on the enhancement of sensitivity of fluorescence detection in CE [89]. They compared the fluorescence intensity and stability for detecting riboflavin using laser or LED as excitation sources and conventional cylindrical optical fiber (COF) and tapered optical fiber (TOF) for conducting the light. LED-

TOF enabled to achieve better LOD and stability than LED-COF, being the sensitivity obtained close to that of Laser-COF (0.8 mM). The LED-TOF-CE method developed was applied to the determination of riboflavin in a green tea sample to demonstrate its suitability in trace analysis.

The simultaneous determination of vitamins has also been studied in the period of time covered by this review. The possibility to minimize interferences from complex samples by optimizing BGE was investigated by Mazina and Gorbatsova [90]. To do that, several extraction procedures and four BGE at pH between 2.1 and 9.5 were tested. The results obtained showed that a two-step extraction (acid hydrolysis followed by enzymatic treatment) and the use of 25 mM phosphoric acid (pH 2.1) as BGE were the most suitable conditions for the determination of different vitamins (thiamine, calcium D-pantothenate, pyridoxine, L-ascorbic acid, nicotinamide, and nicotinic acid) in yeast, beer, and syrups.

The use of on-line preconcentration techniques in order to improve the detection sensitivities of vitamins (pyridoxine, riboflavin, nicotinic acid, and folic acid) was shown by Liu et al. [91]. Namely, they compared the enhancement of sensitivity of three different strategies; normal stacking mode (NSM), field-enhanced sample injection (FESI) and pressure-assisted field-enhanced sample injection (PA-FESI). In the last strategy, negative voltage and positive pressure are simultaneously applied allowing a longer injection time than usual FESI mode. The use of PA-FESI with a water plug as preconcentration technique enabled to increase the peak height of the vitamins from 63 to 172 times (comparing with usual injection), except for riboflavin which cannot be stacked owing to its less electrophoretic mobility. The developed method was applied to the analysis of trace amounts of nicotinic acid (0.75 μg/g) and folic acid (0.21 μg/g) in corns [91].

8. Small organic and inorganic ions

The high efficiency, good repeatability, fast analysis, and low consumption of electrolytes and samples of CE make this technique a good alternative to other more established techniques for individual or multiple determination of small ions. Low molecular ions (organic and inorganic) are present extensively and naturally in many foods and play important roles in several physiological activities [92]. Moreover, low molecular ions (e.g. organic acids) can be added to food products to enhance or modify their color, aroma, flavor, and/or taste, as well as their stability and to control their antibacterial and antioxidant activities. CE methods have extensively been applied to analyze this type of compounds.

For instance, CE analysis of different small organic and inorganic compounds have allowed the classification of wines from different areas [77], the differentiation of unprocessed and processed coconut waters [93], the differentitation of different varieties of lentils [87], the detection of adulterations of olive oils with other vegetable oils such as soy and sunflower oils via CE analysis of trigonelline [94], the differentiation of organic goat's milk from non-organic milk through the determination of their hippuric acid content [95], the monitoring of lactic acid production from sorghum fermentation [96] and the analysis of different alkaloids in beverages [97].

The ratio of citric acid to D-isocitric acid can be used to distinguish authentic and adulterated fruit juices. In a work by Kodama et al., a CE method was developed that allowed the separation and determination of D/L-isocitric and citric acids in fruit juices [98]. In a work by Stage et al., CE was successfully applied to the

determination of melatonin in red and white wine, grape skin and plant extracts of *Salvia officinalis L* [99]. The finding of melatonin, the often called "hormone of darkness" in plants opens an interesting perspective associated to the plethora of health benefits related to the moderate consumption of red wine.

CE with C^4D has shown interesting possibilities for the determination of of carnitine in different types of foodstuffs, namely fruit juices, milk, yogurt, cheese, red meat and chicken meat [100] or for the determination of potassium, sodium, calcium and magnesium in total parenteral nutrition formulations [101]. This method was found to be appropriate for controlling potassium, sodium, calcium and magnesium in parenteral nutrition formulations and successfully applied in daily quality control at the Geneva University Hospitals.

9. Toxins, contaminants, pesticides, and residues

Pathogenic foodborne organisms and their toxins can give rise to significant economic losses to food industry and health systems. Therefore, identifying, monitoring, and quantitating such microorganisms and their toxic products are of paramount importance. CE may represent an interesting alternative to the current microbiological methods for the determination of microbial contaminants in foods. These topics have been recently reviewed in different reports [16, 17].

Due to the dangerous nature of microbial toxins to human and animal health, the presence of these substances in food represents a serious concern worldwide. As a consequence, many countries have set maximum acceptable levels of certain toxins in foods. In addition, new toxins are being identified together with their potential risk to public health. In this regard, it is expected to continue the establishment of new regulatory limits for toxins in foods. Accordingly, there is a demand for reliable

methods that can provide appropriate analysis to enforce legislative limits at acceptable cost and time.

Patulin is a mycotoxin produced by filamentous fungi of the genera *Penicillium*, *Aspergillus* and *Byssochlamys* that mainly contaminates apples, but also other fruits, vegetables bread and meat products. Murillo-Arbizu et al. reported a comparative study between MEKC and HPLC methods for the detection and quantification of patulin [102]. Samples containing patulin were prepared by organic extraction with ethylacetate, but following two different protocols depending on the analytical technique used for the analysis. MEKC analyses were performed using 33.3 mM sodium borate, 66.6 mM SDS and 5% acetonitrile as BGE and bubble cell capillaries with 75 mm I.D. and 56 cm effective length. On the other hand, HPLC analyses were carried out in a ZORBAX Eclipse XDB-C18 column (15 x 0.46 cm, 5 μm particle size) and trifluoroacetic acid 0.1%: acetonitrile (94:6) as mobile phase in isocratic mode. UV detection wavelength in both separation systems was 276 nm. In general, results obtained using both separation systems were comparable with LODs of ca. 0.70 μg/L. Interestingly, the precision obtained with MEKC (RSD 4.0%) was higher than for HPLC (RSD 7.8%) demonstrating good reconditioning of the capillary between runs. The analysis of 20 apple juice samples showed good correlation between both techniques.

Emetic toxin cereulide is produced by the bacteria *Bacillus cereus* in food. Cereulide is a cyclic dodecadepsipeptide, highly hydrophobic, heat-stable and acid/alkali-resistant. The UV detection of cereulide by MEKC has been investigated by Oh and Cox [103]. In their work, artificially contaminated rice with *B. cereus* was extracted with methanol and then diluted in an equal volume of distilled water. During method development stage, the effect of the composition of BGE, pH, SDS concentration,

temperature and voltage was investigated on the resolution, time of analysis and sensitivity. Under optimal separation conditions, cereulide was detected in food samples in less than 10 min with 1.8 and 4.2% RSD values for migration times and peak areas, respectively.

The presence of antibiotics in food is strictly regulated by specific legislation in many countries by the establishment of strict maximum residue limits (MRLs). CE presents a good potential to separate a wide spectrum of these compounds, which is being exploited for the accurate determination of antibiotics in water, milk, meat and related matrices in food analysis. The increased number of reviews and research papers reporting on novel CE methods for the analysis of antibiotics published in the last years indicates a growing interest in the detection of these compounds [5, 10, 13]. The MRLs imposed for many antibiotics are particularly low (μg/kg level). Consequently, a number of novel CE developments are aimed at improving sensitivity in the detection of these substances by different means. For instance, the analysis of fluoroquinolones (FQs) has been investigated using different detection schemes, sample preconcentration and stacking methods [104-110]. Recently, the detection of five quinolones, namely, enoxacin, norfloxacin, ofloxacin, fleroxacin, and pazufloxacin has been approached by CE using potential gradient detection (PGD) in fortified milk samples [104]. PGD is a type of conductivity detection that operates in the direct current mode. The sensitivity with this detection system is not limited by the optical path length since the detection relies on the mobility difference between the analyte and the background co-ion. In their work, Fan et al. investigated the effects of buffer pH and concentration, voltage and addition of bovine serum albumin to the BGE on the separation performance of the quinolones. Under optimal separation conditions, adsorption of the protein onto the silica wall was demonstrated

to improve the response of the analyte by suppression the quinolone-wall interaction and increased EOF velocity, which in turn, led to a shorter analysis time. Using this CE method, the reported LODs were between 0.24 and 0.68 mg/L. In a separate report, a similar instrumental setup was used to develop a novel strategy to improve the sensitivity on the detection of three FQs (rufloxacin, enoxacin and moxifloxacin) [105]. In this case, electrokinetic injection of sample was applied in an acidic BGE to preconcentrate 10-fold the analytes on-line. A detailed study of the parameters affecting the separation and detection demonstrated a significant influence of the eluting power buffer and the analyte-wall interactions on the mobilities of the fluoroquinolones. The same research group has also investigated the simultaneous detection of five FQs (rufloxacin, enoxacin, ciprofloxacin, enrofloxacin, gatifloxacin, and moxifloxacin) by CE with C^4D [106]. The various parameters affecting the sensitivity such as additives, buffer pH and concentration, excitation voltage and frequency were studied. It was found that the FQs extracted from chicken muscle samples by LLE as clean-up and preconcentration procedure were determined with LODs lower than 12 ng/g using an acidic BGE (14 mM sodium acetate, 10 mM tartaric acid and 15% methanol, pH 3.8). Later, Lombargo-Agüí et al. have proposed a CE-LIF method using an SPE and a 325 nm He-Cd laser to determine six commonly used FQs (lomefloxacin, norfloxacin, danofloxacin, sarafloxacin, enrofloxacin and ofloxacin) in water samples [107]. Typical SPE and separation parameters were optimized and the whole analytical procedure was validated using matrix-calibration curves. The proposed method demonstrated good sensitivity, providing LODs from 0.3 (danofloxacin) to 1.9 (norfloxacin) ng/L with RSD values for the migration time below 4.4% (n=30). The detection of FQs in complex food samples has been also investigated by the same research group [108]. The novel approach is based on the

combination of commercial molecularly imprinted polymers (MIP) for SPE and CE-LIF for the sensitive and simultaneous quantification of ciprofloxacin, danofloxacin, enrofloxacin and sarafloxacin. Some steps of the commercially proposed extraction protocol with MIP were modified in order to simplify and reduce the extraction steps. Optimal separation conditions were achieved using 36% of methanol in the BGE (125 mM phosphoric acid, pH 2.8). The analysis of cow raw milk and pig kidney samples spiked with different levels of the four antibiotics served to construct matrix-calibration curves and validate the method. In general, the analytical method provided better LOD, LOQ and RSD values in milk than in kidney samples. Nevertheless, LOQs (below 4 and 35 µg/kg for cow milk and pig kidney, respectively) were much lower than the MRLs established by EU legislation. Recently, He et al. have developed a CE-UV method using field-amplified sample stacking (FASS) for the concentration and separation of nine quinolones [109]. Authors used polymer monolith microextraction based on poly(methacrylic acid-co-ethylene glycol dimethacrylate, PMME) to extract the antibiotics from chicken samples. During the separation method optimization stage, it could be observed that 125 mM phosphate electrolyte (pH 8.7) provided better resolution. The effects of the composition of the acid and organic solvent in the sample solution, sampling time, and voltage on the efficiency of FASS process were systematically investigated. The combined used of PMME and FASS-CE with UV detection demonstrated enrichment factors ranging from 4 to 26 for 9 FQs, indicating the good preconcentration ability of the proposed analytical strategy. In addition, the applicability of the optimized method was demonstrated on chicken meat samples spiked with different concentrations of FQs. The results from these analyses demonstrated the good performance of the method indicating LOQs from 4.6 to 113.3 ng/g.

A novel strategy, based on the combined use of dispersive liquid-liquid microextraction (DLLME) with NACE and UV detection, has been recently explored by Herrera-Herrera et al. for the selective determination of eight FQs in mineral and run-off waters [110]. In DLLME, a suitable combination of an extraction and a disperser solvent has to be rapidly introduced into an aqueous sample and form a cloudy solution that is later centrifuged. Owing to the high surface contact between the sample and the extraction solvent droplets, the extraction equilibrium is quickly achieved. Based on experimental data and central composite design, authors selected pH 7.6, 685 µL of CHCl3 and 1250 µL ACN for extraction. FESI was also implemented with NACE to improve the sensitivity. The baseline separation of a mixture containing different levels of eight FQs was possible in less than 17 minutes with NACE using 3 M acetic acid, 49 mM ammonium acetate in 55:45 v/v methanol:ACN (**Figura 6**). The optimized DLLME-NACE-UV method was applied to analyze spiked and non-spiked water samples. The reported LODs ranged between 1.6 and 15.2 µg/L for mineral water and between 6.6 and 155 µg/L for run-off water.

Sulfonamides are synthetic antibiotics used as therapeutic and prophylactic drugs in animals. Novel CE methods for the detection of these antibiotics have been recently reported. Farooq et al. have developed a CE method for the separation of sulfonamides in meat samples [111]. Four sulfonamides, namely, sulfamethazine, sulfamerazine, sulfadimethoxine, and sulfamethoxazole, were extracted with ACN and cleaned up by SPE. The optimal BGE composition was 45 mM phosphate at pH 6.2. With this CE-UV method, LODs for the analytes under study ranged from 3.7 to 6 µg/kg. Moreover, the applicability of the proposed method was demonstrated by the detection of the antibiotics in chicken and beef meat samples. The detection of sulfonamides and amphenicol-type drugs in poultry tissues has been also attempted by

MEKC-UV in conjunction with SPE [112]. During method development stage, the composition and pH of the buffer was investigated. Optimum conditions were found using a BGE containing 15 mM sodium tetraborate decahydrate (pH 9.3), 25 mM sodium dodecylsulfate and methanol (80:20, v/v). In their study, authors tested different organic solvents and SPE sorbents, namely, C8, C18, Alumina N, and Lichrolut EN in order to eliminate interfering substances from the matrix. Best clean-up conditions were reached with C18 cartridges and pure methanol. The reported LODs of the method ranged between 1.3 ng/g for cloramphenicol and 5.7 ng/g for florfenicol. The effectiveness of the proposed analytical procedure was checked by analyzing tissue samples from the turkeys and hens that were medicated with thiamphenicol or florfenicol. The analyses revealed the presence of the antibiotics in different tissues (muscle, liver and skin) of poultry samples. Recently, a CEC method, with a monolithic column as stationary phase, coupled to MS detection has been developed for the simultaneous separation and identification of nine common sulfonamides in meat samples. LODs ranging from 0.01 to 0.14 μg/L were reached for the studied sulfonamides [113].

The presence of tetracycline antibiotics in food is a cause of concern to consumers and regulatory organizations. This group of broad-spectrum antibiotics is used to prevent or treat mastitis in cows. Ibarra et al. have recently proposed an analytical procedure combining magnetic solid phase extraction (MSPE) and CE-DAD for the quantitative determination of tetracyclines in milk samples [114]. Phenyl-functionalized silica adsorbent was investigated for preparation of magnetic sorbents for MSPE. A study of the affinity and selectivity of the synthesized magnetic adsorbent (Fe_3-O_4-SiO_2-phenyl modified) for tetracyclines showed similar results to those reported using molecular imprinted polymers. The sensitivity of the MSPE-CE

method provided LODs lower than 9 µg/L for tetracyclines (tetracycline, oxytetracycline, doxycycline and chlortetracycline) spiked in milk samples, and intraday RSDs below 2.7% for the migration time.

Lantibiotics are antimicrobial peptides with a variety of biomedical applications that can be present in foods. Their detection in bovine colostrum and predrop beer has been recently approached by MEKC-UV [115]. The ionic strength of phosphate buffer, the concentration of SDS and the pH had a marked influence on the separation of the four lantibiotics (nisin, duramycin, cinnamycin and gallidermin). The optimum conditions for separation of these compounds were obtained with 50 mM phosphate buffer containing 80 mM SDS at pH 3.9. Moreover, the applicability of the proposed method was confirmed by the analysis of three real samples, fermentation broth, bovine colostrum and predrop beer spiked with different levels of the four antibiotics.

Recently, the determination of tilmicosin, erythromycin ethylsuccinate, and clindamycin, using CE has been investigated by Liu et al. [116]. Sensitive detection of these three antibiotics has been achieved using electrochemiluminescence detection with ionic liquid. In the study, the concentration of BMIMBF4, added as ionic liquid, was optimized in order to promote the FASS effect and therefore, increase the sensitivity. Other parameters affecting separation and chemiluminescence detection were systematically investigated. In order to demonstrate the applicability of the proposed method, spiked milk samples with the three antibiotics were extracted with dichloromethane. Optimal separation and chemiluminescence conditions were applied to the detection of the three antibiotics in milk samples in less than 8 min. The LODs of the method were 13, 23, and 3.4 nM for clindamycin, Erythromycin ethylsuccinate, and Tilmicosin, respectively. In a recent report, a novel strategy for preconcentration of different types of antibiotics in milk and their quantitation by CE has been

published [117]. The analytical procedure, based on the protein precipitation with trichloroacetic acid followed by LLE with dichloromethane and SPE in combination with CE-DAD enabled the detection of chloramphenicol, ampicillin, tetracycline, ciprofloxacin and sulfamethoxazol in spiked samples.

Recent applications of CE-MS/MS to the simultaneous quantification of antibiotics in food samples have shown the good possibilities of this type of analytical approaches to the analysis of this type of residues in complex food matrices [118, 119]. For instance, Blasco et al. developed a CE-ESI-IT-MS/MS for qualitative and quantitative determination of eight antibiobiotics and seven pesticides in milk [118]. To achieve this, authors carried out the optimization of the CE separation of the 15 compounds, and then, the most selective, specific and sensitive MS/MS conditions were investigated as well as the extraction conditions. Optimization of the CE separation conditions was carried out using a DAD detector. It was found that 80 mM ammonium acetate/acetic acid buffer at pH 4.6 provided a good compromise between analyte separation and electrical conductivity of the buffer. Sheath liquid composition, flow rate, spray parameters, capillary voltage and fragmentation amplitude were also optimized. The performance of the method was evaluated using milk samples. Analytes were extracted from milk samples using ACN followed by SPE clean-up. Calibration curves based on peak area were linear with correlation coefficient better than 0.992. The LODs were between 1 and 9 µg/kg and RSDs (n=3) of the pesticide and veterinary drug contents were in the range of 2-11%. Another novel CE-MS/MS method has been developed for multiresidue determination of nine penicillins in chicken muscle samples [119]. In this case, a coaxial sheath-liquid sprayer was used for CE-MS coupling. Sample preparation was carried out using extraction with ACN and SPE clean-up. Separation and detection conditions were systematically optimized.

Fragmentation experiments were then performed under the selected conditions. For these analyses, a cut-off of 27% of the precursor mass was set (i.e. the minimum m/z of the fragment ion able to be trapped by the analyzer) and the fragmentation amplitude was manually varied and optimized by monitoring the intensities of the fragment ion. The method provided LODs lower than 12 µg/kg and LOQs below 30 µg/kg in chicken muscle, that are below than the legislated MRLs for this sample type.

The accurate determination of pesticides in fruits, vegetables, and related matrices in food analysis is of great importance. Several novel CE methods are focused on the development of preconcentration strategies. For instance, Rodríguez-Gonzalo et al. developed in-capillary microextraction procedure using monolithic polymers combined with MEKC to sensitively detect carbamate pesticides [120]. The complete analytical procedure involved two steps. In the first one, the sample was loaded onto the sorbent and eluted with methanol into an empty vial. Then, the microextraction capillary was replaced by the separation capillary where the sample is injected and separated. In the study, different monomers were assayed and the performance and effectiveness of the polymeric bed were investigated in terms of length and sample flow rate. Polydivinylbenzene-based polymer provided higher preconcentration in shorter times than butyl methacrylate polymers. For the MEKC-DAD analysis, a capillary of 75 µm x 50 cm (effective length) was used. The BGE used was an aqueous solution of 60 mM SDS and 5 mM sodium tetraborate. Separations were carried out at 30 kV and 30 ºC. Under these conditions, good separation of methomyl, asulam, carbendazim, aldicarb, carbetamide, propoxtur, piricarb, carbaryl, carbofuran and methiocarb pesticides in less than 6 min was achieved. The procedure allowed the enrichment of the target pesticides from aqueous samples with a mean

preconcentration factor of 60. Moreno-González et al. investigated the use of DLLME and sweeping-MEKC to simultaneously determine up 12 pesticides, namely, carbendazim, oxamyl, methomyl, benomyl, asulam, baygon, carbofuran, aldicarb, carbaryl, promecarb, methiocarb, and napropamid, in juices samples [121]. Optimal sweeping-MEKC conditions were established using 100 mM boric acid, pH 9.0, 50 mM SDS and 5% of ACN as BGE, a separation voltage of 27 kV and 27 ºC as separation temperature. Sweeping preconcentration step was performed injecting the sample diluted in BGE without SDS during 25 s at 35 mbar. A systematic study of the parameters affecting DLLME procedure provided the best extracting conditions of the pesticides from juice samples. The usefulness of this methodology was evaluated in banana, pineapple and tomato juice containing the pesticides at concentrations between 5 and 500 µg/L. Calculated LODs ranged between 1 and 7 µg/L in juice samples. A recent work by Barahona et al. has demonstrated the good possibilities of using hollow fiber-liquid-phase microextraction in combination with CE for the determination of a group of three fungicides (i.e. thiabendazole, carbendazim and imazalil) in orange juices [122]. Analytes were extracted from samples through a supported liquid membrane of 2-octanone into 20 µl of a stagnant aqueous solution of 10 mM HCl inside the lumen of the hollow fiber. Subsequently, the acceptor solution was directly subjected to analysis by CE-DAD. Using this technique, a good separation of the selected analytes was achieved in 13 min. In spite of this, a comparison with LC-MS demonstrated better sensitivity of the later technique for the detection of the three fungicides. The application of MS detection coupled to CE has been also investigated to the analysis of vegetable extracts for the detection of organophosphorus pesticides, namely, dimethoat, trichlorphon, glyphosate [123]. In their study, authors used (ICP)-MS to perform the analysis of the compunds in two

steps. First, the qualitative analysis of the pesticides was carried out and, then, a second step for quantification was developed. Optimum resolution was attained with 150 mM $Na_2B_4O_7$, 50 mM H_2BO_3 and 20 mM SDS, pH 8.5. Two peristaltic pumps were used for the qualitative determination of the pesticides by CE-ICP-MS analysis. The first pump was used to transport the CE eluent to second pump, and the later pump was used to send makeup solution to nebulizer in order to introduce analyte solution into ICP-MS and achieve stable atomization efficiency. For quantitative analysis, a collective sample-introduction system was implemented to improve peak shapes, sensitivity and fluctuation of baseline of the three pesticides. This procedure allowed the detection of pesticides in cabbages providing LODs lower than 0.07 µg/mL. Flutolanil, simazine, haloxyfop, acifluofen, dinoseb, picloram, and ioxynil pesticides were analyzed by CE-ESI-MS in fruits [124]. To achieve that, PLE was applied using hot water at 60ºC and 1500 psi, followed by SPE clean-up. Optimal conditions were established with 35 mM ammonium formate (pH 9.7) as BGE, 20 ºC as capillary temperature and 23 kV as applied voltage in uncoated fused-silica capillary. Under these separation conditions, herbicides were separated in 12 min with reported LODs below 0.1 µg/mL. The applicability of the method was tested on 120 fruit samples including melon, watermelon, apricot and peaches.

10. Food additives

Food preservatives are added to foods to prevent alteration and degradation by microorganisms during storage. However, excessive addition of preservatives such as sorbic acid, benzoic acid and their salts may induce allergic contact dermatitis, convulsion and hives. Therefore, the development of convenient and inexpensive

analysis methods of these additives is of great importance for food safety. The possibilities of CE to analyze food additives have been further demonstrated through the numerous papers published on this topic in the reviewed period. CE with online preconcentration and contactless conductivity detection has been applied for the sensitive determination of sorbic and benzoic acids in soy sauce [125]. CE with UV detection has also been applied to determine different benzoic acids in natural matrices used as Chinese medicines [126], while CE with AD has been demonstrated suitable for the determination of food preservatives such as methylparaben, ethylparaben, propylparaben, butylparaben, potassium sorbate and sodium lactate [127]. Seven food grade antioxidants (propyl gallate, octyl gallate, dodecyl gallate, butylated hydroxyanisole, butylated hydroxytoluene, tert-butylhydroquinone and alpha-tocopherol) plues the synthetic preservatives sorbic acid, benzoic acid, salicylic acid and the parabens were resolved by MEEKC in 11 min using a low pH microemulsion containing 20% propan-2-ol. The method was successfully applied to noodles for the determination of butylated hydroxytoluene and propyl gallate and to pharmaceutical supplement tablets for alpha-tocopherol determination [128].

The possibilities of CE to analyze other type of additives were further demonstrated through the analysis of artificial sweeteners such as aspartame, cyclamate, saccharin and acesulfame-K in soft drinks and tabletop sweetener formulations using CE with C^4D [129]. Although most food colorants are expected to be safe, several food colorants have demonstrated some toxicity. As a consequence, many countries have established regulations for the use of natural and synthetic colorants in foods. Due to these regulatory restrictions, new methods are demanded for rapid detection and identification of colorants in food products. Following this trend, a home made CE equipment with linear charge coupled device for visible light absorption detection was

developed for the determination of food dyes in fruit juices and candies. A computer program that converts the spectral data after each run into the electropherograms was developed to evaluate the analytical parameters. The dyes selected for analytical evaluation of the system were Brilliant Blue FCF, Fast Green FCF, Sunset Yellow FCF, and Amaranth [130].

11. Food interactions and processing

Manufacture, processing or storage can originate undesired changes on food composition. For that reason, the development of analytical techniques to study the modification of the chemical composition of foods in order to guarantee their safety and quality is of importance in Food Science and Technology.

5-Hydroxymethylfurfural (HMF) is formed as intermediate product during the Maillard reaction and from hexoses degradation and caramelization. It has been identified in a wide variety of heat-processed foods and has been used as indicator to assess the severity of heat treatment and food freshness and quality. Although some studies have shown that HMF is cytotoxic, genotoxic, mutagenic and carcinogenic, others suggest that it does not pose a serious health risk [131, 132]. The analysis of HMF along with melamine in ten commercial milk samples using MEKC-UV was carried out by Chen and Yang [131]. Lately, a MEKC-UV method has been applied to the determination of HMF in foodstuffs with matrices of different nature (breakfast cereals, toasts, honey, orange juice, apple juice, jam, coffee, chocolate, and biscuits) and at different concentration levels [132]. This method was proposed by the authors as an alternative to the LC-UV official method for the analysis of HMF in food.

Taylor and Woonton demonstrated the influence of the milk treatment on the yield and glycosylation characteristics of glycomacropeptide [133]. The authors

investigated the effect of five different heat treatments on the quantity and carbohydrate content of glycomacropeptide fraction isolated from milk by using a CZE method to separate and quantify the carbohydrates released.

An interesting chiral MEKC method based on the use of SDS as surfactant and hydroxypropyl-β-cylodextrin was developed by Gotti et al. to study the thermal epimerisation of epi-structured catechins to non-epi-structured catechins and to analyze tea samples of different geographical origins having different storage conditions and manufacturing processes [134]. By using a multivariate study, the analyzed tea samples were discriminated in function of the content of (-)-gallocatechin and (-)-catechin, which were considered as indices of improper storage conditions and/or thermal degrading processes. Besides, the authors considered the content of (-)-epigallocatechin gallate as an index of high native biological value of the edible product.

The effect of the storage conditions in foods has been investigated in the period of time covered in this review. Thus, Sugimoto et al. profiled amino and organic acids by CE-MS and quantified free sugars by LC-MS, in order to study the metabolomics profiles and the sensory characteristic of edamame (preparation of immature soybeans in the pod) stored for different temperatures and lengths [135]. Refrigerated storage has been also studied to evaluate possible changes in the content of bioactive substances and nutritional values of cactus pear [136]. Besides analysing total soluble solids, flesh humidity, fruit loss of weight, antiradical activity and total content of polyphenols, the authors employed CE to determine the content of vitamin C. The results obtained demonstrated that under refrigerated conditions (8°C for 3 and 4 weeks), this fruit preserves its nutritional properties.

On the other hand, Cheung et al. investigated the stability of folic acid during the main stages of fortified instant fried noodle manufacturing using a simple CZE method [137]. They demonstrated the high stability of this vitamin throughout the process which could be used to enhance folate intakes through fortification.

A sensitive analysis of bovine β-lactoglobulin of three different infant foods (whose main components were fruit, fish or meat) on purpose contaminated with dairy desserts and submitted to thermal treatment to simulate potential contamination in the manufacturing line, was carried out by Peláez-Lorenzo et al. [39]. To do that, the authors developed a new sample preparation method based on the use of a disrupting agent, a reducing compound and high saline concentration as extraction solution and a CE-LIF method to analyze this allergenic protein. Since levels of contamination of one part of yoghurt in 10000 parts of baby food could be detected, the method can be considered as a powerful tool in quality control of baby food samples.

Lately, Koyama et al. have determined the optimum growth period for accumulating functional phenols in germinated buckwheat (soaked in darkness) and buckwheat sprouts (cultivated by hydroponic culture) [138]. CE was used to measure the rutin content in germinated buckwheat whereas HPLC was employed to analyze issorientin, orientin, isovitexin, vitexin and rutin from buckwheat sprouts.

12. Chiral analysis of food compounds

CE is very useful for chiral analysis due to its high efficiency and flexibility for using a great variety of chiral selectors in small amount. A variety of recent reviews are focused on the use of enantiomeric separation using capillary electomigration techniques [11, 15, 139-142]. Chiral separation plays a significant role in food

science. It has been used, among others applications in quality control, monitoring of food processing, adulterations, evaluation of safety, etc.

The ratio of citric acid to D-isocitric acid was used to assess fruit juice authentication [98]. For this purpose citric acid was separated from isocitric acid enantiomers using D-quinic acid as a chiral selector in ligand exchange CE with UV detection. Among the six different metal tested as central ions (Fe(III), Co(II), Ni(II), Cu(II), Zn(II) and Mn(II)), Ni(II) gave the best response in terms of resolution and sensitivity with LOD of 3 μg/mL.

CE-IT-MS coupling was used for the determination of D and L-carnitine in a variety of dietary supplements (different beverages, biscuits, capsules and tablets) [143]. The low concentration of the chiral selector used in the BGE (0.2% succinyl-γ-CD) was compatible with MS detection (without the need of partial filling technique) obtaining a LOD of 10 ng/mL, that enabled the determination of up to 0.025% of D isomer. Derivatization with FMOC prior to CE-MS analysis was necessary in order to achieve a chiral separation with succinyl-γ-CD (**Figure 7**). A new CE-IT-MS method was developed for the analysis of the non-protein amino acid ornithine in beers [144]. In this case, samples were derivatized with FITC to facilitate stereoselective interaction with the chiral selector γ-CD. The obtained LOD of 2.5 nM was largely improved compared to that obtained with UV detection using similar analytical conditions [145].

13. Other applications

CE methods can also be employed to analyze other kind of compounds in foods. For instance, CZE methods with LIF or AD have been used for the determination of different low-molecular mass aldehydes in different food samples [146, 147]. Thus, a

sensitive CZE method with LIF was used for the determination of formaldehyde, acetaldehyde, propionaldehyde, butyraldehyde, valeraldehyde, glyoxal and methyl glyoxal in ozonated drinking water. Using a precolumn derivatization of these compound with fluorescein 5-thiosemicarbazide (FTSC) was possible to reach LODs from 0.15 to 0.35 ng/L which are 1000 times lower than those specified by legislation (in the μg/L range) [146]. CE with AD was also helpful for determining nine aldehydes, namely six monoaldehydes (formaldehyde, acetaldehyde, propanal, butanal, pentanal, hexanal) and three dialdehydes (glutaradehyde, 2,3-butanedione and methylgloxal), which were derivatized with 2-thiobarbituric (TBA), in wines, oils and water-soaked products. By using this methodology, without additional sample pretreatment, recoveries from 82.8 to 123.8 % and LODs between 0.008 and 0.074 mg/L were achieved [147].

Carnitine is a chiral non-protein amino acid. The L-enantiomer plays an important role in the metabolism of fatty acids, but the D-enantiomer has been found to have a considerable toxic influence on biochemical processes. Although small amounts of L-carnitine are produced in the human body from lysine and methionine, it is mainly introduced by food intake. Porsmsila et al developed a CE method with C^4D to quantify L-carnitine in different foodstuff including fruit juices eliminating the need for derivatization [100]. However, this methodology does not allow a differentiation between enantiomers as done by Sánchez-Hernández et al who employed an EKC method coupled to MS detection to the determination of both enantiomers in dietary food supplements, namely drinks, biscuits, capsules and tablets [143].

Glucosinolates are present in high concentration in plants from Brassica family. Since some studies have shown that a diet rich in them may reduce the risk of certain cancers there is an increased interest in the health benefits from the content of glucosinolates in these vegetables. Thus, the quantification of intact glucoraphin in broccoli (seeds and florets) and Brussels sprouts was carried out using a MEKC-UV method based on the use of sodium cholate as micellar phase without a SPE cleanup step [148]. Under optimal conditions the determination of glucoraphin was carried out in about 5 min with LODs from 0.1 to 4 mg/100 g which are 10-100 times lower than the levels typically found in these vegetables.

Alkaloids has been also analyzed in foods by different CE methods. Meinhart et al. optimizated a MEKC method for caffeine quantification in decaffeinated coffees using theobromine as internal standard [149]. Chen et al. developed a CEC method with a hybrid monolithic column with octyl and sulfonic acid groups and UV detection for analyzing theophylline and caffeine in carbonated drinks, juices and tea [97].

A pressurized CEC method with AD was developed to separate and determine five phenolic xenoestrogens in chicken eggs and milk powder samples [150]. These compounds are endocrine-disrupting chemicals which have adverse health effects and can enter the food chain as food contaminants. For that reason, the development of analytical methods to their determination in food is necessary. Thus, Wu et al. developed a method based on the use of ACN: 5 mM Tris at pH 8.0 (60:40 v/v) as mobile phase, 6 kV as applied voltage, and 7 MPa as supplementary pressure, which enabled the separation of xenoestrogens in about 20 min with LODs ranging from 2 to 50 ng/mL, and satisfactory recoveries (79.2-102.6 %) [150].

14. CE microchip technology in food analysis

Miniaturization is another important trend adopted by many food laboratories. The beneficial features of microchip-CE technology include the capability for fast and automatized analysis in situ, and, negligible consumption of reagents and samples. During the period covered by this review, excellent reviews have appeared in the literature dealing with novel advances on CE chips [151-153]. The emergent development of microchips is corroborated by the recent applications of microchip CE in food analysis.

Commercial instruments based on lab-on-a-chip technology have received wide acceptance in food analysis laboratories. In recent years, this technology has been helpful in solving a variety of authentication problems in food analysis. For instance, lab-on-a-chip CE has been used with PCR and SNaPshot technology in order to analyze *trnL* intron polymorphisms, a genetic marker useful for the identification of the botanical origin of plant oils [154]. Using single –base primer extension assay, the discrimination of olive and avocado DNA targets, differing by only one base, was possible. Fruit juice authentication has been also investigated using PCR heteroduplex assay, PCR restriction fragment length polymorphism (RFLP) and lab-on-a-chip CE to analyze plastid DNA sequences. The methodology allowed the detection of grapefruit and mandarin juice in orange juice [155]. In addition to plastid DNA, mitochondrial markers serve to solve authentication issues. Particularly, a region in the 12S rRNA gene has been investigated as molecular marker for the identification of game and domestic meats using RFLP and lab-on-a-chip CE [156]. The methodology involves the generation and detection of characteristic restriction patterns that enable the rapid identification of meat species. Using the same commercial CE instrument, Coïsson et al. have recently analyzed DNA extracts

amplified by multiplex PCR, previously isolated from cooked meat balls and soups, in order to detect traces of celery and sesame DNA [157]. Similarly, Delibato et al. have developed a PCR-lab-on-a-chip method to detect the foodborne microorganism *Listeria monocytogenes* in food samples [158]. Lab-on-a-chip has been recently compared with conventional CGE for the analysis of soybean [159]. Authors concluded both techniques were adequate for quantification of the relative amount of protein fractions in samples to demonstrate their different genetic origin. Chemometric analysis of electrophoretic profiles demonstrated to be a powerful method to discriminate between soybean varieties providing suitable datasets for the statistical analysis.

Recent advances on microchip CE for food analysis have been directed to the development of novel detection systems in order to improve the sensitivity, selectivity and ease of manipulation [29, 160-163]. An interesting application of the use of end-channel amperometric detectors in microchip CE for the analysis of BAs in double malt dark beers was described by Dossi et al [29]. In this work, ED was developed by depositing ruthenium-containing films on glassy carbon electrodes placed at the end of the microchip separation channel. ED has been also coupled to microchip MEKC for the analysis of tetracycline antibiotics [160]. The microdevice was designed to contain two microchannels for two sequential preconcentration steps, FASS and FESI. Several electrode compositions based on different graphite powder and cellulose-dsDNA proportions, were tested for amperometric detection of the analytes. A variety of parameters, including buffer concentration, water plug length, preconcentration time, sample injection time, SDS concentration, and the distance between the electrode an the channel outlet, were evaluated and optimized. Using this method, tetracycline, doxycycline, oxytetracycline and chlortetracycline were detected in less

than 200 s. Sensitivity improvements close to 11000-fold for the detection of the four tetracyclines in standard samples were calculated using FASS and FESI preconcentration steps prior to the separation process. The applicability of the analytical procedure was confirmed by the analysis of spiked Korean beef meat samples. Recently, Du and Fung have designed a new dual electrode detection cell to enable easy replacement of the electrodes in microchip CE [161]. The working electrode was fabricated using carbon-fiber micro-disk electrode and the detection setup was designed with an exchangeable modular concept by bringing two PMMA plates together using screws. Separation was performed using a running buffer comprised of 20 mM sodium tetraborate and 2 mM β-CD in 7% methanol at pH 9.0, The voltage applied for the separation was 12 kV across the separation capillary with high voltage Pt electrode place in the inlet vial and grounded Pt electrode in the outlet plastic together within the dual electrode cell setup. Five polyphenols (trans-resveratrol, (+)-catechin, (-)-epicatechin, quercetin and gallic acid, present in red wine analyzed using the developed CE chip. The use of current ratio at +1.0V/+0.8V demonstrated the ability of the method to distinguish overlapping peaks and, therefore, to asses polyphenol peak purity in red wine samples.

Ohla et al. developed and applied a novel microchip CE system using deep UV fluorescence detection with a 266-nm laser for the analysis of dopamine, serotonin, tryptophan tyrosine, and salsolinol in banana [162]. To achieve this, fused silica glass microchips with a cross injector layout was used for fluorescence detection. In addition to this CE chip, a monolith integrated glass emitter with incorporated makeup-flow channels close to the emitter resembling the coaxial sheath-flow sprayer was fabricated for the coupling with a single quadrupole MS. The application of the CE chip-MS to the analysis of banana extracts allowed reliable peak assignment. On

the other side, the compounds that exhibit native fluorescence after excitation in the deep UV spectral region below 290 nm, were sensitively detected without the necessity for complex sample preparation and derivatization in less than 1 minute (**Figure 8**). The procedure allowed the study of the composition of certain compounds found in banana in different ripening states.

Quantum dots (QD) are crystal particles with good photochemical stability, high luminescent and tunable excitation/fluorescence wavelength at different particle sizes. In addition to these advantages, the interaction of quantum dots with compounds such as organophosphorus pesticides, leading to an enhancement of the fluorescence, makes their application to the detection of pesticides very promising. According to this, a novel fluorescence detection strategy, based on laser-induced fluorescence detection and the use of quantum dots has been investigated by Chen and Fung for the analysis of organosphosphorus pesticides in vegetables [163]. Authors used thermal sol-gel transition process to attain stable and repeatable base layer for self-assembly of QD onto the inner capillary wall surface at the detection zone. A 450 mm capillary was mounted in a microfluidic device unit. Parameters affecting MEKC separation, namely, buffer pH and composition, SDS concentration and methanol concentration were investigated. Under optimum conditions, mevinphos, methidathion, diazinon, phosalone pesticides were selectively detected in spiked tomato samples with LODs between 0.05 and 0.18 mg/kg.

15. Foodomics and other future trends of CE in food analysis

Our group has coined and defined for the first time in a SCI journal the new discipline of Foodomics [2, 3, 164]. Namely, Foodomics has been defined as a discipline that studies the food and nutrition domains through the application of advanced omics

technologies to improve consumer's well-being, health, and confidence. Thus, Foodomics is intended to be not only an useful concept, but more importantly, it is intended to be a global discipline that includes all of the emerging working areas in which food (including nutrition), advanced analytical techniques (mainly omics tools), and bioinformatics are combined. Nowadays, it can be observed how nutrition research is moving from classical epidemiology and physiology studies to molecular biology including global omics approaches in order to understand how bioactive food compounds interact with genes affecting transcription factors, protein expression and metabolite production. In this context, Foodomics can help to elucidate how diet can influence human health. The Foodomics study of these complex interactions requires the development of advanced analytical approaches combined with bioinformatics [165] in which CE is expected to play a crucial role. Thus, to carry out all these studies Transcriptomics, Proteomics and Metabolomics approaches [166] have to be developed together with an adequate integration of the information that they provide, ideally following a holistic approach as systems biology [167].

Foodomics also covers e.g., the development and monitoring of new transgenic foods using molecular tools [84], the metabolomic study of foods toward compounds profiling [26], the metabolomic study of the efficacy of antioxidant supplementation (N-acetyl-L-cysteine) with strenuous physical exercise [168], microbial metabolomics [169] or new investigations on food functions via nutrigenomics or nutrigenetics approaches [165]. In this context, CE-MS has already shown to provide important contributions for metabolomics studies of transgenic corn [170] or proteomics studies of transgenic soy [45]. Besides, based on the previous applications in clinical studies [171], CE-MS is expected to provide impressive possibilities in the discovery of biomarkers allowing the study of molecular food functions, or the identification of

specific metabolites useful for food authentication, traceablity or quality [172]. In this regard, the use of high resolution mass analyzers (TOF, FTMS, QTOF, etc) will be crucial to obtain accurate mass measurements for the determination of elemental compositions of metabolites and to carry out tentative identification based on metabolites databases.

Great possibilities are also expected from the combination of chiral analysis and CE-MS [173]. On the other hand, in order to conveniently fulfil all the expectations derived from the use of CE-MS in food analysis and Foodomics, it is expected that new technological advances, mainly new instrumental configurations of the interface, will make this technique more robust and user-friendly. Moreover, the impressive potential of CGE-LIF for nucleic acids analysis, as already demonstrated through the Human Genome Project, can provide important information at different levels including genomics, transcriptomics and/or epigenetics in Foodomics studies.

The number of applications relative to the use of microchips in food analysis has also grown. Thus, chip electrophoresis combined with native fluorescence was applied to analyze active banana ingredients with label-free detection [162]. Namely, dopamine and serotonin, their precursors tryptophan and tyrosine and also the isoquinoline alkaloid salsolinol were detected in banana in less than 1 min. Besides, after 10 days of ripening, the compound levodopa which is a metabolite of the tyrosine pathway was also found. For reliable peak assignment, the compounds were also analyzed by coupling chip electrophoresis with mass spectrometry. This paper demonstrates the applicability of chip electrophoresis with native fluorescence detection for rapid analysis of natural compounds in fruits and reveals the potential of chip-based separation systems for the analysis of complex food mixtures. Other recent applications of chip electrophoresis in food analysis include the analysis of phenolic

compounds in beer [174], the detection of celery and sesame in different foods including meat balls and commercial soup via DNA analysis [157], the direct detection of melamine in milk products [175] or the detection of nitrite in ham and sausage samples [176]. These applications are good examples of the huge possibilities of chip electrophoresis in monitoring the quality of different foods. In this regard, the use of CE-microchips and their new instrumental approaches including the development of new coatings compatible with microchips [177, 178] are also expected to keep finding important and new applications in the food analysis domain [179, 180]. In the near future, it is expected that novel CE separation and detection approaches applicable to food analysis and Foodomics will keep developing and finding new application in these exciting fields of research.

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16. References

[1] Bernal, J., Mendiola, J.A., Ibáñez, E., Cifuentes, A., *J. Pharm. Biomed*. 2011, *55*, 758-774.

[2] Herrero, M., García-Cañas, V., Simo, C., Cifuentes, A., *Electrophoresis* 2010, *31*, 205-228.

[3] Herrero, M., Simó, C., García-Cañas, V., Ibáñez, E., Cifuentes, A., *Mass Spectrom. Rev*. 2011, DOI 10.1002/mas.

[4] Guo, L.H., Qiu, B., Xiao, X.Y., Chen, G.N., *Food Sci. Biotechnol*. 2009, *18*, 823-832.

[5] Rodríguez-Robledo, V., Smyth, W.F., *Electrophoresis* 2009, *30*, 1647-1660.

[6] Ravelo-Pérez, L.M., Asensio-Ramos, M., Hernández-Borges, J., Rodríguez-Delgado, M.A., *Electrophoresis* 2009, *30*, 1624-1646.

[7] Asensio-Ramos, M., Hernandez-Borges, J., Rocco, A., Fanali, S., *J. Sep. Sci.* 2009, *32*, 3764-3800.

[8] Valls, J., Millán, S., Martí, M.P., Borrás, E., Arola, L. *J. Chromatogr. A*, 2009, *1216*, 7143-7172.

[9] Pyrzyska, K., Biesaga, M., *Trends Anal. Chem*. 2009, *28*, 893-902.

[10] García-Campaña, A.M., Gámiz-Gracia, L., Lara, F.J., Iruela, M.D., Cruces-Blanco, C., *Anal. Bioanal. Chem*. 2009, *395*, 967-986.

[11] Herrero, M., Simó, C., García-Cañas, V., Fanali, S., Cifuentes, A., *Electrophoresis* 2010, *31*, 2106–2114.

[12] Hurtado-Fernandez, E., Gómez-Romero, M., Carrasco-Pancorbo, A., Fernández-Gutiérrez, A., *J. Pharm. Biomed. Anal.* 2010, *53*, 1130-1160.

[13] Castro-Puyana, M., Crego, A.L., Marina, M.L., *Electrophoresis* 2010, *31*, 229-250.

[14] Viglio, S., Fumagalli, M., Ferrari, F., Iadarola, P., *Electrophoresis* 2010, *31*, 93-104.

[15] Simó, C., García-Cañas, V., Cifuentes, A., *Electrophoresis* 2010, *31*, 1442-1456.

[16] Vallejo-Cordoba, B., González-Córdova, A.F., *Electrophoresis* 2010, *31*, 2154-2164.

[17] Shin, G.W., Hwang, H.S., Chung, B., Jung, G.Y., *Electrophoresis* 2010, *31*, 2137-2153.

[18] Kumar, A., Malik, A.K., Picó, Y., *Electrophoresis* 2010, *31*, 2115-2125.

[19] Chen, X.J., Yang, F.Q., Wang, Y.T., Li, S.P., *Electrophoresis* 2010, *31*, 2092-2105.

[20] Lara, F.J., García-Campaña, A.M., Velasco, A.I., *Electrophoresis* 2010, *31*, 1998-2027.

[21] Ramautar, R., Somsen, G.W., de Jong, G.J., *Electrophoresis* 2010, *31*, 44-54.

[22] Mala, Z., Gebauer, P., Bocek, P., *Electrophoresis* 2011, *32*, 116-126.

[23] Rodríguez-Ramírez, R., González-Córdova, A.F., Vallejo-Corboda, B., *Anal. Chim. Acta* 2011, *685*, 120-126.

[24] Christodouleas, D., Fotakis, C., Economou, A., Papadopoulos, K., Timotheou-Potamia, M., Calokerinos, A., *Anal. Letters* 2011, *44*, 176-215.

[25] Ignat, I., Volf, I., Popa, V.I., *Food Chem*. 2011, *126*, 1821-1835.

[26] García-Cañas, V., Simo, C., Leon, C., Ibañez, E., Cifuents, A., *Mass Spectrom. Rev*. 2011, *30*, 396-416.

[27] Zinellu, A., Sotgia, S., Bastianina, S., Chessa, R., Gaspa, L., Franconi, F., Deiana, L., Carru, C., *Amino Acids* 2009, *36*, 35-41.

[28] Baskan, S., Tezcan, F., Kose, S., Oztekin, N., Erim, F.B., *Electrophoresis* 2010, *31*, 2174-2179.

[29] Dossi, N., Toniolo, R., Pizzariello, A., Susmel, S., Bontempelli, G., *Electrophoresis* 2011, *32*, 906-912.

[30] De Andres, F., Zougagh, M., Castañeda, G., Ríos, A., *Electrophoresis* 2010, *31*, 2165-2173.

[31] Wang, X., Chen, Y., *J. Chromatogr. A* 2009, *1216*, 7324-7328.

[32] Xin, H., Stone, R., *Science* 2008, *322*, 1310-1311.

[33] Xia, J., Zhou, N., Liu, Y., Chen, B., Wuc, Y., Yao, S., *Food Control* 2010, *21*, 912-918.

[34] Sun, H., Liu, N., Wang, L., Wu, Y., *Electrophoresis* 2010, *31*, 2236–2241.

[35] Wen, Y., Liu, H., Han, P., Gao, Y., Luan, F., Li, X., *J. Sci. Food Agric.* 2010, *90*, 2178-2182.

[36] Meng, L., Shen, G., Hou, X., Wang, L., *Chromatographia* 2009, *70*, 991-994.

[37] Klampfl, C.W., Andersen, L., Haunschmidt, M., Himmelsbach, M., Buchberger, W., *Electrophoresis* 2009, *30*, 1743-1746.

[38] Hsu, Y-H., Chen, K-T., Liu, Y-W., Hsieh, S-H., Huang, H-Y., *Anal. Chim. Acta* 2010, *673*, 206-211.

[39] Peláez-Lorenzo, C., Diez-Masa, J.C., Vasallo, I., de Frutos, M., *Anal. Chim. Acta* 2009, *649*, 202-210.

[40] Vallejo-Cordoba, B., Rodríguez-Ramírez, R., González-Córdova, A.F., *Food Chemistry* 2010, *120*, 304-307.

[41] Salmanowicz, B.P., *Electrophoresis* 2010, *31*, 2226-2235.

[42] Montealegre, C., Marina, M.L., García-Ruiz, C., *Electrophoresis* 2010, *31*, 2218-2225.

[43] Delgado, F.J., Rodríguez-Pinilla, J., González-Crespo, J., Ramírez, R., Roa, I., *Int. J. Food Sci. Techn.* 2010, *45*, 512–519.

[44] Catala-Clariana, S., Benavente, F., Giménez, E., Barbosa, J., Sanz-Nebot, V., *Anal. Chim. Acta* 2010, *683*, 119-125.

[45] Simó, C., Domínguez-Vega, E., Marina, M.L., García, M.C., Dinelli, G., Cifuentes, A., *Electrophoresis* 2010, *31*, 1175–1183.

[46] Stalikas, C.D., in: Uppu, R.M., Pryor, W.A., Murthy, S.N., Parinandi, N.L. (Eds.), Free Radicals and Antioxidant Protocols, Vol. 610. Springer-Verlag, New York, LLC 2009, Chapter 5.

[47] Carrasco-Pancorbo, A., Gómez-Caravaca, A.M., Segura-Carretero, A., Cerretani, L., Bendini, A., Fernández-Gutiérrez A., *J. Sci. Food Agric*. 2009, *89*, 2144-2155.

[48] Lerma-García, M.J., Lantano, C., Chiavaro, E., Cerretani, L., Herrero-Martínez, J.M., Simó-Alfonso, E.F., *Food Res. Int*. 2009, *42*, 1446-1452.

[49] Ballus, C.A., Meinhart A.D., Bruns R.E., Godoy, H.T., *Talanta* 2011, *83*, 1181-1187.

[50] Berzas Nevado, J.J., Castañeda Peñalvo, G., Rodríguez Robledo, V., Vargas Martínez, G., *Talanta* 2009, *79*, 1238-1246.

[51] Berzas Nevado, J.J., Castañeda Peñalvo, G., Rodríguez Robledo, V., *Talanta* 2010, *82*, 548–554.

[52] García-Villalba, R., Carrasco-Pancorbo, A., Vázquez-Martín, A., Oliveras-Ferraros C., Menéndez, J.A., Segura-Carretero, A., Fernández-Gutiérrez A., *Electrophoresis* 2009, *30*, 2688-2701.

[53] Gómez-Caravaca, A.M., Carrasco-Pancorbo, A., Segura-Carretero, A., Fernández-Gutiérrez A., *Electrophoresis* 2009, *30*, 3099-3109.

[54] Hsiao, H-Y., Chen, R.L.C., Cheng, T-J., *Food Chem*. 2010, *120*, 632-636.

[55] Peres, R.G., Tonin, F.G., Tavares, M.F.M., Rodriguez-Amaya, D.B., *Food Chem*. 2011, *127*, 651-655.

[56] Chi, L., Li, Z., Dong, S., He, P., Wang, Q., Fang, Y., *Microchim. Acta* 2009, *167*, 179-185.

[57] Cesla, P., Fischer, J., Jandera, P., *Electrophoresis*, 2010, *31*, 2200-2210.

[58] Li, Z., Haung, D., Tang, Z., Deng, C., *J. Sep. Sci.* 2010, *33*, 1079-1084.

[59] Uysal, U.D., Aturki, Z., Raggi, M.A., Fanali, S., *J. Sep. Sci.* 2009, *32*, 1002-1010.

[60] Peres, R.G., Micke, G.A., Tavares, M.F.M., Rodriguez-Amaya, D.B., *J. Sep. Sci.* 2009, *32*, 3822-3828.

[61] Nicolaou, I.N., Kapnissi-Christodoulou, C.P., *Electrophoresis* 2010, *31*, 3895-3902.

[62] Du, F., Fung, Y.S., *Electrophoresis* 2010, *31*, 2192-2199.

[63] Zhang, Q.F., Li, S.C., Lai, W.P., Cheung, H.Y., *Food Chem.* 2009, *113*, 684-691.

[64] Lee, I.S.L., Boyce, M., Breadmore, M.C., *Food Chem*. 2011, *127*, 797-801.

[65] Fukuji, T.S., Tonin, F.G., Tavares, M.F.M., *J. Pharm. Biomed. Anal*. 2010, *51*, 430-438.

[66] Vaher, M., Matso, K., Levandi, T., Helmja, K., Kaljurand, M., *Procedia Chem*. 2010, *2*, 76-82.

[67] Helmja, K., Vaher, M., Püssa, T., Kaljurand, M., *J. Chromatogr. A* 2009, *1216*, 2417-2423.

[68] Dong, S., Chi, L., HE, P., Wang, Q., Fang, Y., *Talanta* 2009, *80*, 809-841.

[69] Chu, Q.C., Jiang, L.M., Ye, J.N., *J. Anal. Chem*. 2010, *65*, 103-108.

[70] Sawalha, S.M.S., Arráez-Román, D., Segura-Carretero, A., Fernández-Gutiérrez, A., *Food Chem*. 2009, *116*, 567-574.

[71] Chen, X.J., Zhao, J., Meng, Q., Li, S.P., Wang, Y.T., *J. Chromatogr. A* 2009, *1216*, 7329-7335.

[72] Xia, L., Sun, Z.W., Li, G.L., Suo, Y.R., You, J.M., *Eur. Food Res. Technol.* 2010, *230*, 715-722.

[73] Albrecht, S., Schols, H.A., Klarenbeek, B., Voragen, A.G.J., Gruppen, H., *J. Agric. Food Chem.* 2010, *58*, 2787-2794.

[74] Tezcan, F., Gültekin-Özgüven, M., Diken, T., Özçelik, B., Erim, B., *Food Chem*. 2009, *115*, 873-877.

[75] Tezcan, F., Kolayli, S., Ulusoy, H. S-E., Erim, F.B., *J. Food Nutr. Res.* 2011, *50*, 33-40.

[76] Gürel, A., Hizal, J., Öztekin, N., Erim, F.B., *Chromatographia* 2006, *64*, 321-324.

[77] Rovio, S., Sirén, K., Sirén, H., *Food Chem.* 2011, *124*, 1194-1200.

[78] Rovio, S., Yli-Kauhaluoma, J., Siren, H., *Electrophoresis* 2007, *28*, 3129-3135.

[79] Alekseeva, A.V., Kartsova, L.A., Kazachishcheva, N.V., *J. Anal. Chem*. 2010, *65*, 202-208.

[80] Nogueira, T., Lucio do Lago, C., *J. Sep. Sci*. 2009, *32*, 3507-3511

[81] Yang, Z., Li, A., Zhu, J., Wang, Q., He, P., Fang, Y., *J. Sep. Sci.* 2010, *33*, 1312-1318.

[82] Holck, A., Pedersen B.O., Heir, E., *Eur. Food Res. Technol.* 2010, *231*, 475-483.

[83] Holck A., Dromtorp, S.M., Heir, E., *Eur. Food Res. Technol.* 2009, *230*, 185-194.

[84] García-Cañas, V., Mondello, M., Cifuentes, A., *Electrophoresis* 2010, *31*, 2249-2259.

[85] García-Cañas, V., Mondello, M., Cifuentes, A., *J. Sep. Sci.* 2011, *34*, 1011-1019.

[86] Guo, J., Yang, L., Chen, L., Morisset, D., Li, X., Pan, L., Zhang, D., *Anal. Chem.* 2011, *83*, 1579-1586.

[87] Uysal, U.D., Oncu-Kaya, E.M., Tunçel, M., *Chromatographia*, 2010, *71*, 653-658.

[88] Yu, C-Z., He, Y-Z., Xie, H-Y., Gao, Y., Gan, W-E., Li, J., *J. Chromatogr. A* 2009, *1216*, 4504-4509.

[89] Yang, X., Huo, F., Yuan, H., Zhang, B., Xiao, D., Choi, M.M.F., *Electrophoresis* 2011, *32*, 268-274.

[90] Mazina, J., Gorbatsova, J., *Procedia Chem*. 2010, *2*, 46-53.

[91] Liu, Q., Liu, Y., Guan, Y., Jia, L., *J. Sep. Sci*. 2009, *32*, 1011-1017.

[92] Merusi, C., Corradini, C., Cavazza, A., Borromei, C., Salvadeo, P., *Food Chem*. 2010, *120*, 615-620.

[93] Naozuka, J., da Veiga, M.A.M.S., Richter, E.M., Paixao, T.R.L.C., Angnes, L., Oliveira, P.V., *Food Anal. Meth.* 2011, *4*, 49-56.

[94] Sánchez-Hernández, L., Puchalska, P., García-Ruiz, C., Crego, A.L., Marina, M.L., *J. Agric. Food Chem*. 2010, *58*, 7489-7496.

[95] Carpio, A., Rodríguez-Estévez, V., Sánchez-Rodríguez, M., Arce, L., Valcárcel, M., *Electrophoresis* 2010, *31*, 2211-2217.

[96] Schober, T.J., Bean, S.R., Wang, D., *Cereal. Chem*. 2009, *86*, 117-121.

[97] Chen, M.L., Zheng, M.M., Feng, Y.Q., *J. Chromaotgr. A* 2010, *1217*, 3547-3556.

[98] Kodama, S., Taga, A., Yamamoto, A., Ito, Y., Honda, Y., Suzuki, K., Yamashita, T., Kemmei, T., Aizawa, S., *Electrophoresis* 2010, *31*, 3586-3591.

[99] Stege, P.W., Sombra, L.L., Messina, G., Martínez, L.D., Silva, M.F., *Electrophoresis* 2010, *31*, 2242-2248.

[100] Pormsila, W., Krahenbuhl, S., Hauser, P.C., *Electrophoresis* 2010, *31*, 2186-2191.

[101] Nussbaumer, S., Fleury-Souverain, S., Bouchoud, L., Rudaz, S., Bonnabry, P., Veuthey, J.L., *J. Pharm. Biomed*. 2010, *53*, 130-136.

[102] Murillo-Arbizu, E., González-Peñas, E., Amézqueta, S., *Food Chem. Toxicol*. 2010, *48*, 2429-2434.

[103] Oh, M.H., Cox, J.M., *J. Food Safety* 2010, *30*, 652-665.

[104] Qin, W., Liu, Q., Fan, Y., *J. Sep. Sci.* 2009, *32*, 118-124.

[105] Fan, Y., Tian, Z., Qin, W., *Anal. Lett.* 2009, *42*, 1057-1069.

[106] Yang, Z., Qin, W., *J. Chromatogr. A* 2009, *1216*, 5327-5332.

[107] Lombardo-Agui, M., Gámiz-Gracia, L., García-Campaña, A.M., Cruces-Blanco, C., *Anal. Bioanal. Chem*. 2010, *396*, 1551-1557.

[108] Lombardo-Agüí, M., García-Campaña, A.M., Gámiz-Gracia, L., Cruces-Blanco, C., *J. Chromatogr. A.* 2010, *1217*, 2237-2242.

[109] He, H.B., Lv, X.X., Yu, Q.W., Feng, Y.Q., *Talanta* 2010, *82*, 1562-1570.

[110] Herrera-Herrera, A.V., Hernández-Borges, J., Borges-Miquel, T.M., Rodríguez-Delgado, M.A., *Electrophoresis* 2010, *31*, 3457-3465.

[111] Farooq, M.U., Su, P., Yang, Y., *Chromatographia* 2009, *69*, 1107-1111.

[112] Kowalski, P., Plenis, Al., Oledzka, I., Konieczna, L., *J. Pharm. Biomed. Anal.* 2011, *54*, 160-167.

[113] Cheng, Y-J., Huang, S-H., Singco, B., Huang, H-Y., J. Chromatogr. A. DOI: 10.1016/j.chroma.2011.06.027.

[114] Ibarra, I.S., Rodríguez, J.A., Miranda, J.M., Vega, M., Barrado, E., *J. Chromatogr. A* 2001, *1218*, 2196-2202.

[115] Stanley, B., Mehr, K.A., Kellock, T., Van Hamme, J.D., Donkor, K.K., *J. Sep. Sci.* 2009, *32*, 2993-3000.

[116] Liu, Y.M., Shi, Y.M., Liu, Z.L., Peng, L.F., *J. Sep. Sci.* 2010, *33*, 1305-1311.

[117] Vera-Candioti, L., Olivieri, A., Goicoechea, H.C., *Talanta* 2010, *82*, 213-221.

[118] Blasco, C., Picó, Y., Andreu, V., *Electrophoresis* 2009, *30*, 1698-1707.

[119] Bailón-Pérez, M.I., García-Campaña, A.M., Iruela, M.D., Cruces-Blanco, C., Gámiz Gracia, L., *Electrophoresis* 2009, *30*, 1708-1717.

[120] Rodríguez-Gonzalo, E., Ruano-Miguel, L., Carabias-Martínez, R., *Electrophoresis* 2009, *30*, 1913-1922.

[121] Moreno-González, D., Gámiz-Gracia, L., García-Campaña, A.M., Bosque-Sendra, J.M., *Anal. Bioanal. Chem*. 2011, *400*, 1329-1338.

[122] Barahona, F., Gjelstad, A., Pedersen-Bjergaard, S.P., Rasmussen, K.E., *J. Chromatogr. A* 2010, *1217*, 1989-1994.

[123] Yang, G., Xu, X.Q., Shen, M.C., Wang, W., Xu, L.J., Chen, G.N., Fu, F.F., *Electrophoresis* 2009, *30*, 1718-1723.

[124] Juan-García, A., Font, G., Juan, C., Picó, Y., *Food Chem.* 2010, *120*, 1242-1249.

[125] Wei, R.X., Li, W.H., Yang L.R., Jiang, Y.X., Xie, T.Y., *Talanta* 2011, *83*, 1487-1490.

[126] Gao, S.Y., Li, H., Wang, L., Yang, L.N., *J. Chin. Chem. Soc.* 2010, *57*, 1374-1380.

[127] Wang, W.Y., Wang, Y.P., Zhang, J.B., Chu, Q.C., Ye, J.N., *Anal. Chim. Acta* 2010, *678*, 39-43.

[128] Darji, V., Boyce, M.C., Bennett, I., Breadmore, M.C., Quirino, J., *Electrophoresis* 2010, *31*, 2267-2271.

[129] Bergamo, A.B., Fracassi da Silva, J.A., Pereira de Jesus, D., *Food Chem*. 2011, *124*, 1714-1717.

[130] Fraige, K., Assuncao, N.A., Pinto, R.D., Carrilho, E., *J. Liq. Chromatogr. Relat. Technol.* 2009, *32*, 1862-1878.

[131] Chen, Z., Yan, X., *J. Agric. Food Chem.* 2009, *57*, 8742-8747.

[132] Teixidó, E., Núñez, O., Santos, F.J., Galceran, M.T., *Food Chem*. 2011, *126*, 1902-1908.

[133] Taylor, C.M., Woonton, B.W., *Int. Dairy J*. 2009, *19*, 709-714.

[134] Gotti, R., Furlanetto, S., Lanteri, S., Olmo, A., Ragaini, V., *Electrophoresis* 2009, *30*, 2922-2930.

[135] Sugimoto, M., Goto, H., Otomo, K., Ito, M., Onuma, H., Suzuki, A., Sugawara, M., Abe, S., Tomita, M., Soga, T., J. *Agric. Food Chem*. 2010, *58*, 8418-8425.

[136] Nazareno, M.A., Coria Cayupán, Y., Targa, G., Ochoa, J., *Acta Hort. ISHS* 2009, *811*, 131-135.

[137] Cheung, R.H.F., Hughes, J.G., Marriot, P.J., Small, D.M., *Food Chem*. 2009, *112*, 507-514.

[138] Koyama, M., Nakamura, C., Nakamura, K., J. *Food Sci. Technol*. DOI 10.1007/s13197-011-0316-1

[139] Preinerstorfer, B., Lammerhofer, M., Lindner, W., *Electrophoresis* 2009, *30*, 100-132.

[140] Scriba, G.K.E. *J. Pharm. Biomed. Anal*. 2011, *55*, 688-701.

[141] Lu, H.A., Chen, G.N., *Anal. Methods* 2011, *3*, 488-508.

[142] Caslavska, J., Thormann, W. *J.Chromatogr. A* 2011, *1218*, 588-601.

[143] Sánchez -Hernández, L., Castro-Puyana, M., García-Ruiz, C. Crego, A.L., Marina, M.L., *Food Chem.* 2010, *120*, 921-928.

[144] Domínguez-Vega, E., Sánchez-Hernandez, L., García-Ruiz, C., Crego, A.L., Marina, M.L., *Electrophoresis* 2009, *30*, 1724-1733.

[145] Domiguez-Vega, E., Martínez-Girón, A.B., García-Ruiz, C., Crego, A.L., Marina, M.L., *Electrophoresis* 2009, *30*, 1037-1045.

[146] Baños, C.E., Silva, M., *Electrophoresis* 2010, *31*, 2028-2036.

[147] Zhang, J-B., Li, M-J., Li, W-L., Chu, Q-C., Ye, J-N., *Electrophoresis*, 2011, *32*, 705-711.

[148] Lee, I., Boyce, M.C., Breadmore, M.C., *Anal. Chim. Acta* 2010, *663*, 105-108.

[149] Meinhart A.D., Schaper Bizzotto, C., Ballus, C.A., Prado, M.A., Bruns R.E., Teixeira Filho, J., Godoy, H.T., *Food Chem.* 2010, *120*, 1155-1161.

[150] Wu, W., Yuan, X., Wu, X., Lin, X., Xie, Z., *Electrophoresis* 2010, *31*, 1011-1018

[151] Pumera, M., Escarpa, A., *Electrophoresis* 2009, *30*, 3315-3323.

[152] Kailasa S.K., Kang, S.H., *Sep. Purific. Rev*. 2009, *38*, 242-288.

[153] Lim Y.C., Kouzani, A.Z., Duan, W., *Microsyst. Technol.* 2010, *16*, 1995-2015.

[154] Spaniolas, S., Bazakos, C., Spano, T., Zoghby, C., Kalaitzis, P., *Food Chem.* 2010, *122*, 850-856.

[155] Scott, M., Knight, A., *J. Agric. Food Chem*. 2009, *57*, 4545-4551.

[156] Fajardo, V., González, I., Dooley, J., Garret, S., Brown, H.M., García, T., Martín, R., *J. Sci. Food Agric*. 2009, *89*, 843-847.

[157] Coïsson, J.D., Cereti, E., Garino, C., D'Andrea, M., Recupero, M., Restani, P., Arlorio, M., *Food Res. Int.* 2010, *43*, 1237-1243.

[158] Delibato, E., Gattuso, A., Minucci, A., Auricchio, B., De Medici, D., Toti, L., Castagnola, M., Capoluongo, E., Gianfranceschi, M.V., *J. Sep. Sci.* 2009, *32*, 3817-3821.

[159] Blazek, V., Caldwell, R.A., *Int J. Food Sci. Technol*. 2009, *44*, 2127-2134.

[160] Lee, K.S., Park, S.H., Won, S.Y., *Electrophoresis* 2009, *30*, 3219-3227.

[161] Du, F., Fung, Y.S., *Electrophoresis* 2010, *31*, 2192-2199.

[162] Ohla, S., Schulze, P., Fritzsche, S., Belder, D., *Anal. Bioanal. Chem.* 2011, *399*, 1853-1857.

[163] Chen, Q, Fung, Y., *Electrophoresis* 2010, *31*, 3107-3114.

[164] Cifuentes A., *J. Chromatogr. A* 2009, *1216*, 7109.

[165] García-Cañas, V., Simó, C., Leon, C., Cifuentes, A., *J. Pharmaceut. Biomed.* 2010, *51*, 290–304.

[166] Simó, C., Ibáñez, C., Gómez-Martínez, A., Ferragut, J.A., Cifuentes, A., *Electrophoresis* DOI: 10.1002/elps.201100019.

[167] Oh, E., Hasan, M.N., Jamshed, M., Park, S.H., Hong, H.M., Song, E.J., Yoo, Y.S., *Electrophoresis* 2010, *31*, 74-92.

[168] Lee, R., West, D., Phillips, S.M., Britz-McKibbin, P., *Anal. Chem*. 2010, *82*, 2959-2968.

[169] Wang, Z., Ma, X., Chen, X., Zhao, X., Chen, T., *Prog. Chem*. 2010, *22*, 163-172.

[170] Leon, C., Rodríguez, I., Lucio, M., Garcia-Cañas, V., Ibañez, E., Schmitt-Kopplin, P., Cifuentes, A., *J. Chromatogr. A* 2009, *1216*, 7314-7323.

[171] Mischak, H., Schanstra, J.P., *Proteomics Clin. Appl.* 2011, *5*, 9-23.

[172] Ramautar, R., Mayboroda, O.A., Somsen, G.W., de Jong, G.J., *Electrophoresis* 2011, *32*, 52-65.

[173] Giuffrida, A., León, C., García-Cañas, V., Cucinotta, V., Cifuentes, A., *Electrophoresis* 2009, *30*, 1734-1742.

[174] Cheng, H.Y., Chen, S.C., Lee, H.L., *J. Chinese Chem. Soc*. 2010, *57*, 371-377.

[175] Zhai, C., Qiang, W., Sheng, J., Lei, J.P., Ju, H.X., *J. Chromatogr. A* 2010, *1217*, 785-789

[176] Shiddiky, M.J.A., Lee, K.S., Son, J., Park, D.S., Shim, Y.B., *J. Agric. Food Chem*. 2009, *57*, 4051-4057.

[177] Bernal, J., Sánchez-Hernández, L., Elvira, C., Velasco, D., Ibáñez, E., Cifuentes, A., *J. Sep. Sci.* 2009, *32*, 605–612.

[178] Herrero, M., Bernal, J., Velasco, D., Elvira, C., Cifuentes, A., *J. Chromatogr. A* 2010, *1217*, 7586–7592.

[179] Liu, B.Y., Jin, Q.H., Zhang, Y., Mayer, D., Krause, H.J., Zhao, J.L., Offenhausser, A., *Michrochim. Acta* 2011, *172*, 193-198

[180] Kovachev, N., Canals, A., Escarpa, A., *Anal. Chem*. 2010, *82*, 2925-2931.

Figure captions

Figure 1. MEKC-LIF electropherogram of (A) a sardine extract and (B) a sardine extract spiked with biogenic amines. Peak identification: 1, tryptamine; 2, tyramine; 3, cadaverine; 4, spermidine; 5, histamine; 6, putrescine. Redrawn from [28] with permission from Willey-VCH.

Figure 2. CE-TOF base peak electropherogram of the digested protein extract from conventional and transgenic soybean. Redrawn from [45] with permission from Willey-VCH.

Figure 3. CZE Electropherogram of 13 phenolic compounds from extra-virgin olive oil. Peak identification: 0, solvent; 1, oleuropein glycoside; 2, tyrosol; 3, hydroxytyrosol; 4, cinnamic acid; 5, luteolin; 6, apigenin; 7, ferulic acid; 8, caffeic acid; 9, *p*-coumaric acid; 10, vanillic acid; 11, 3,4-dihydroxybenzoic acid; 12, gallic acid; 13, *p*-hydroxybenzoic acid. Redrawn from [49] with permission from Elsevier.

Figure 4. Electropherograms of (A) hydrolysed coffee samples without adulteration, (B) contaminated by 10% w/w of coffee husks, and (C) contaminated by 10% w/w of corn grain. Peak identification: xy, xylose; fr, fructose; ma: mannose; ar, arabinose; gl, glucose; ga, galactose. Redrawn from [80] with permission from Willey-VCH.

Figure 5. CGE-LIF electrophoregrams of MLGA reactions of a sample containing 1% MON810, 1% MON863, and 1% GA21 maize DNA obtained under different MLGA reaction conditions. (A) non-optimal ligation conditions, (B) optimal ligation conditions. Peak identification: ga21, GA21 maize DNA; mon863, MON863 maize DNA; mon810, MON810 maize DNA; and, adh, reference DNA. Redrawn from [84].

Figure 6. DLLME-NACE-UV electropherogram of (A) run-off water sample spiked with the fluoroquiniloes (FQs) (concentration: 2500 mg/L of Lomefloxacin, 2000

mg/L of levofloxacin, 2000 mg/L of marbofloxacin, 112.5 mg/L of IS (pipemidic acid), 2500 mg/L of ciporfloxacin, 2000 mg/L of sarafloxacin, 250 mg/L of enrofloxacin, 500 mg/L of danofloxacin and 250 mg/L of difloxacin); (B) a nonspiked run-off water sample. Redrawn from [110] with permission from Willey-VCH.

Figure 7. CE-MS/MS extracted ion electropherogram and the corresponding MS/MS spectra for the peaks of L- and D-carnitine obtained from a biscuit sample. Redrawn from [143] with permission from Elsevier.

Figure 8. (A) Microchip CE-fluorescence detection of a banana extract in a later ripening state. (B) Calibration plot of serotonin with concentrations in the micromolar range (n=4). Peak identification: 1, Serotonin; 2, dopamine; 3, salsolinol; 4, tryptophan; 5, tyrosine; 6, levodopa. Redrawn from [162] with permission from Springer.

Table 1. Review papers on capillary electromigration methods used for food analysis and Foodomics published in the period covered by this work (February 2009-February 2011).

Subject	Publication year	Reference
CE and Microchip CE for Detection of Genetically Modified Organisms	2009	[4]
CE-MS for trace analysis of food contaminants	2009	[5]
Food safety and food quality applications of CE-MS	2009	[6]
Miniaturized separation techniques for food analysis	2009	[7]
Separation methods (including CE) of food anthocyanins, isoflavonces and flavanols	2009	[8]
Analysis of phenolic acids and flavonoids in honey (including CE)	2009	[9]
CE to the determination of antibiotics in food and environmentalsamples	2009	[10]
Chiral CE in food analysis	2010	[11]
CE methods to determine antioxidant phenolic compounds	2010	[12]
CE and CEC analysis of antibiotics in food (and other) matrices	2010	[13]
MEKC analysis of amino acids	2010	[14]
Chiral CE-MS	2010	[15]
CE for the analysis of contaminants	2010	[16]
CE methods for detection of food-borne pathogens	2010	[17]
Sample preparation methods for the determination of pesticides in foods using CE-UV and CE-MS	2010	[18]
CE and CEC of nucleosides and nucleotides in foods	2010	[19]
Applications of CE coupled to chemiluminescence	2010	[20]
Applications of SPE coupled to CE	2010	[21]
Applications of CE using sample stacking	2011	[22]
Authentication and traceability of foods from animal origin by PCR-based capillary electrophoresis	2011	[23]
Flow-Based Methods (including CE) with Chemiluminescence Detection for Food Analysis	2011	[24]
Methods (including CE) for characterisation of polyphenolic compounds in fruits and vegetables	2011	[25]
MS-based analytical methodologies (including CE) for genetically modified crops characterization	2011	[26]

Figure 1

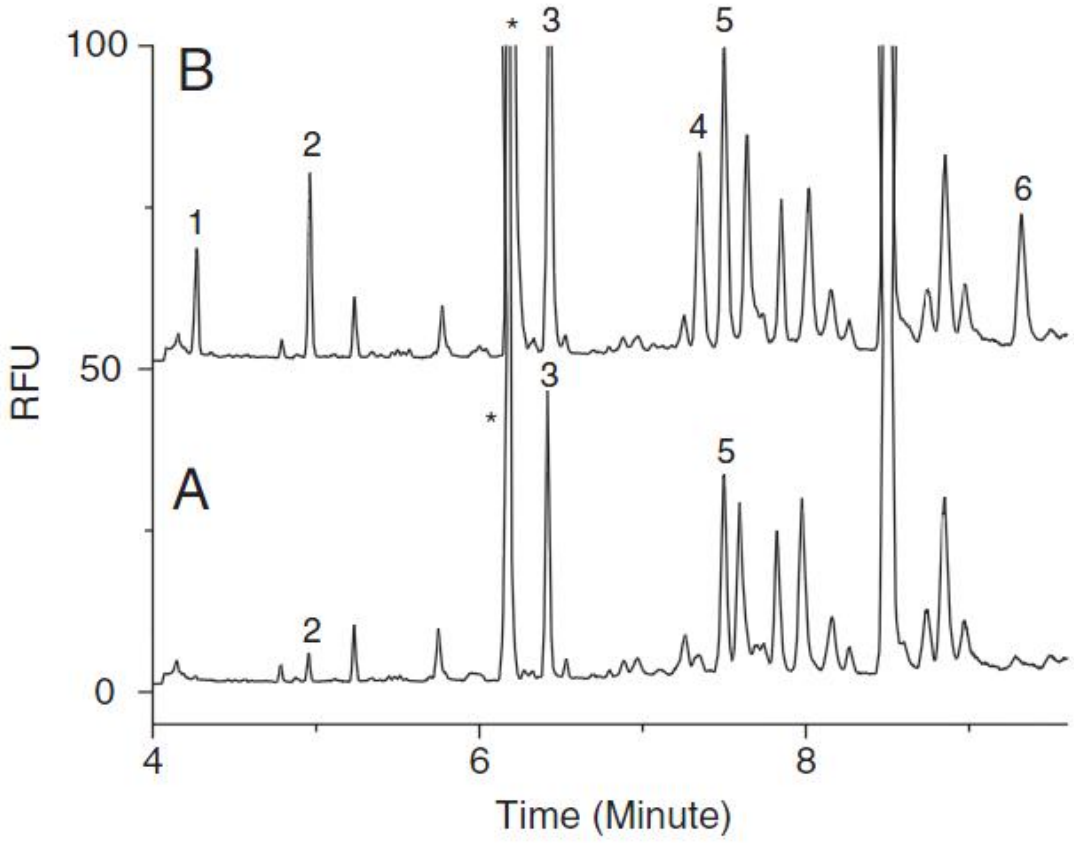
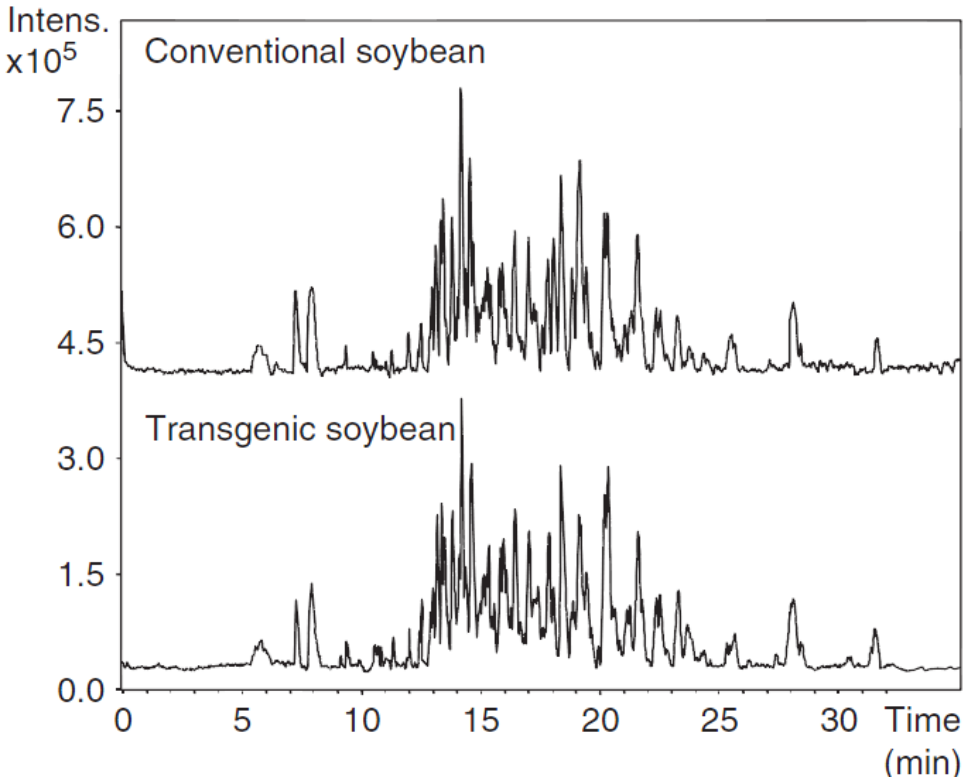


Figure 2


Intens.
x10^5
Conventional soybean
7.5
6.0
4.5
Transgenic soybean
3.0
1.5
0.0
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5
10
15
20
25
30
Time
(min)

Figure 3

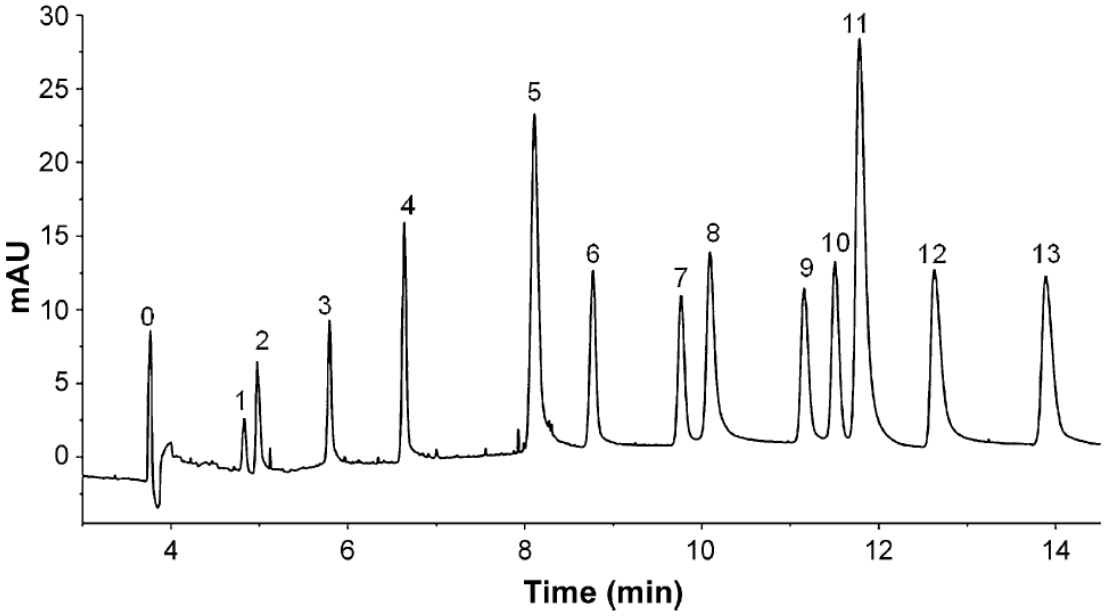
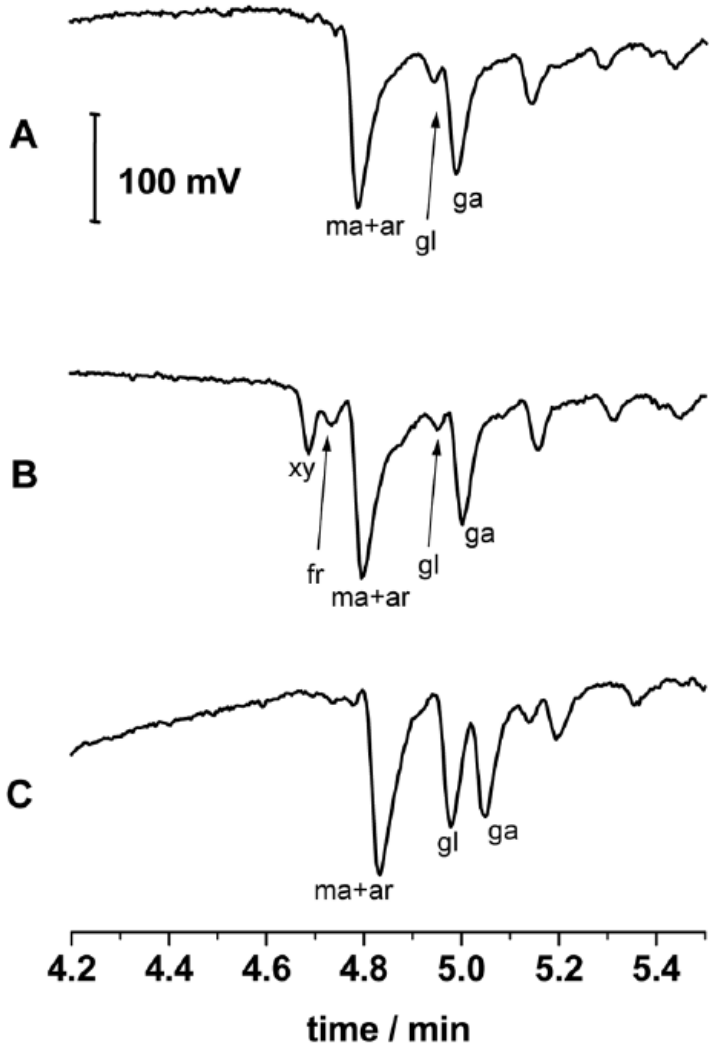


Figure 4


A
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gl
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B
xy
fr
ma+ar
gl
ga
C
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4.2
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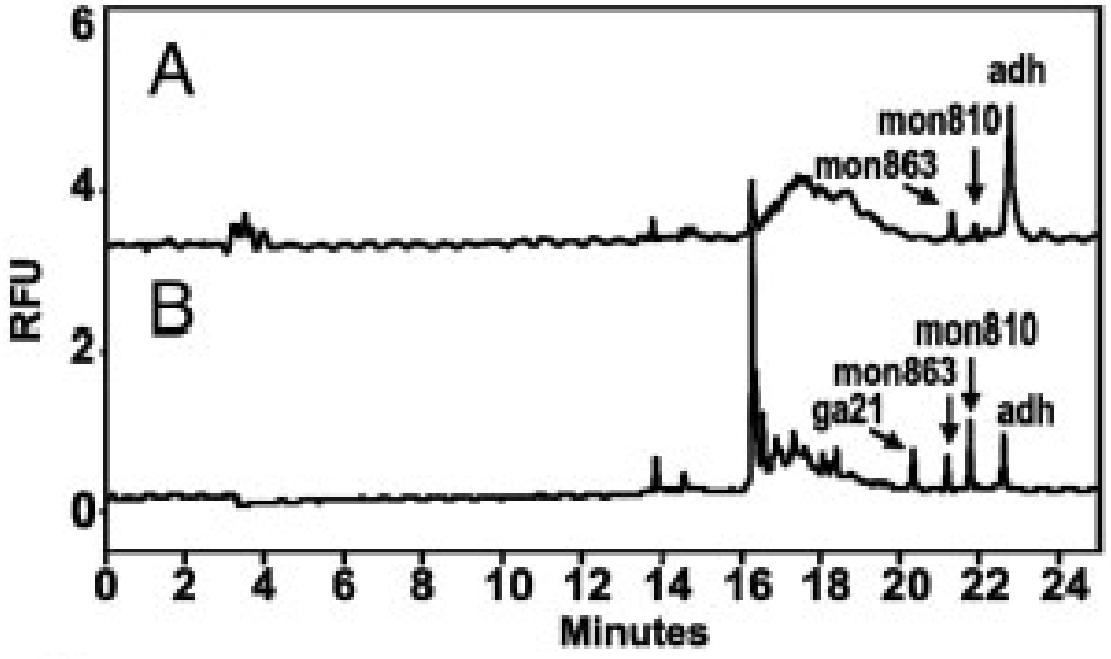
5.2
5.4
time / min

Figure 5


A
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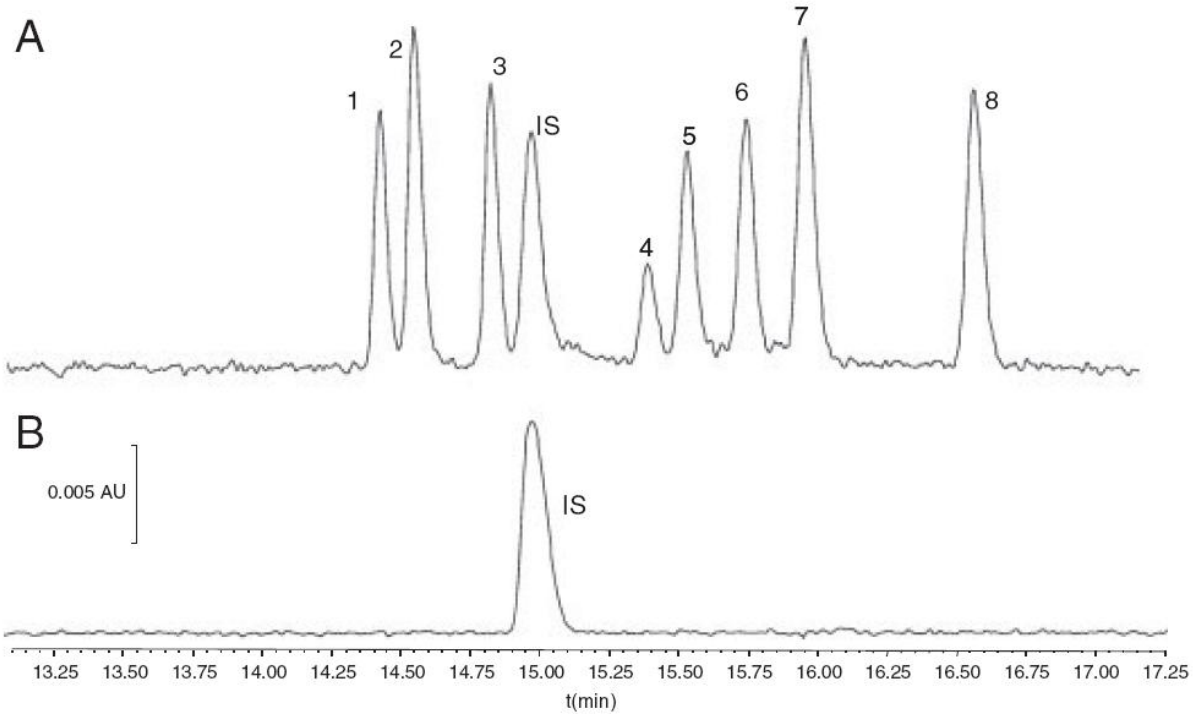
0 2 4 6 8 10 12 14 16 18 20 22 24
Minutes

Figure 6


A
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B
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13.25
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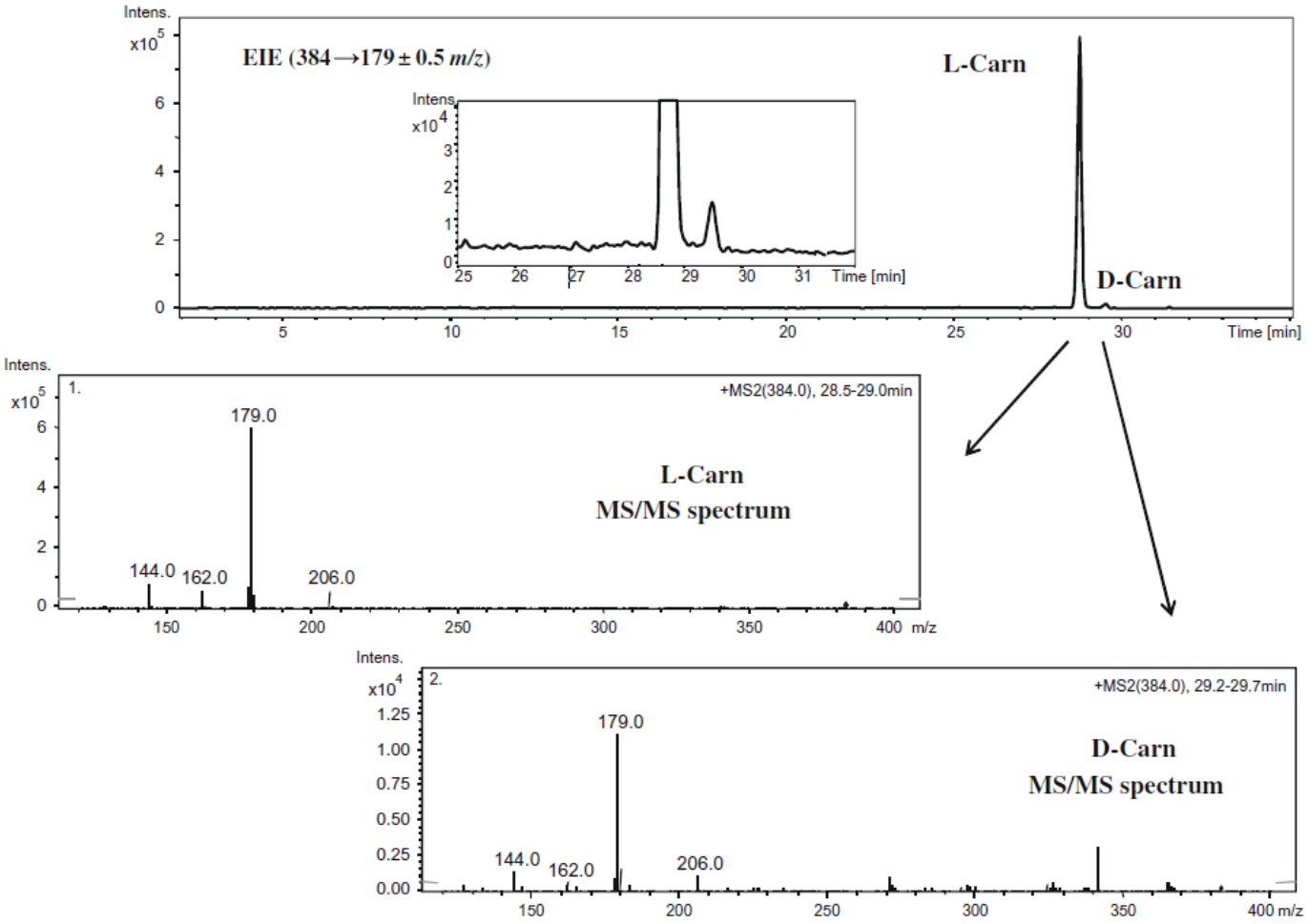
t(min)

Figure 7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x10^5
EIE (384 → 179 ± 0.5 m/z)
Intens.
x10^4
Time [min]
L-Carn
D-Carn
Time [min]
Intens.
x10^5
1.
+MS2(384.0), 28.5-29.0min
179.0
144.0
162.0
206.0
L-Carn
MS/MS spectrum
m/z
Intens.
x10^4
2.
+MS2(384.0), 29.2-29.7min
179.0
144.0
162.0
206.0
D-Carn
MS/MS spectrum
m/z
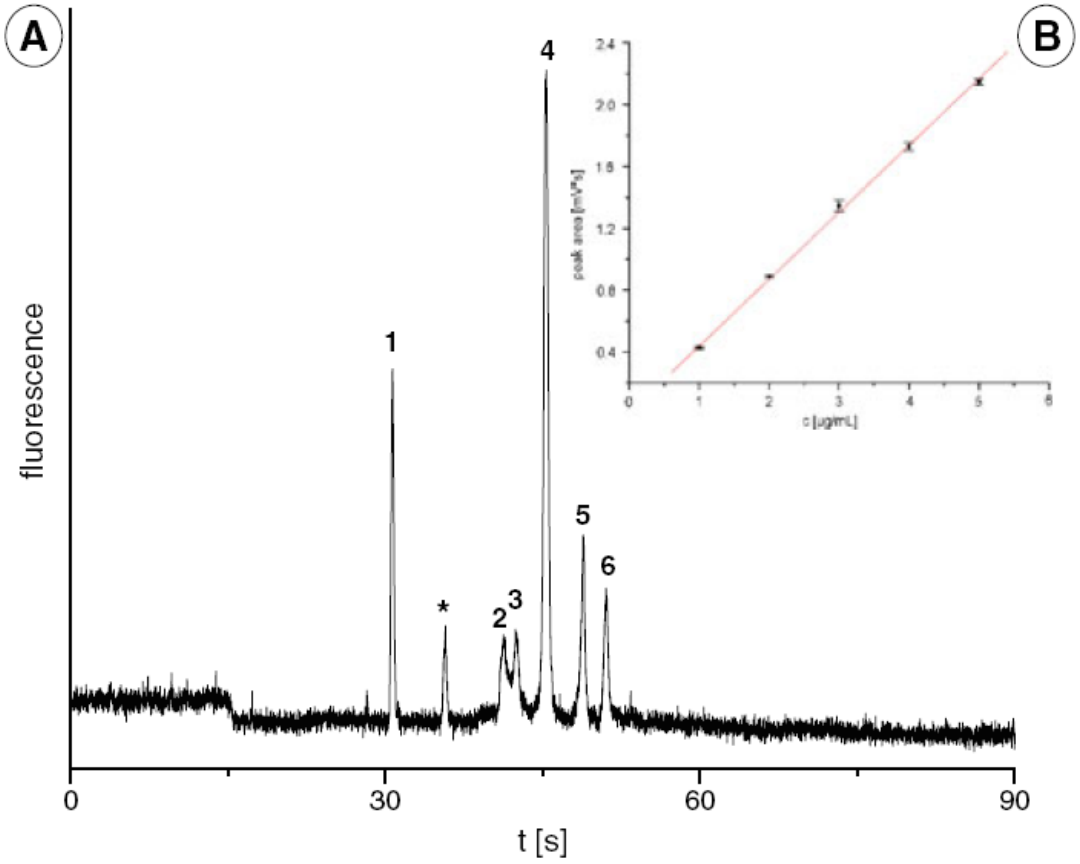
Figure 8